

## **UNITED STATES AIR FORCE RESEARCH LABORATORY**

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### **NEAR-INFRARED ULTRASHORT PULSE LASER BIOEFFECTS STUDIES**

Clarence P. Cain  
Gary D. Noojin  
David J. Stolarski

Northrop Grumman Information Technology  
4241 Woodcock Drive, Ste. B-100  
San Antonio, TX 78228

Robert J. Thomas  
Benjamin A. Rockwell

**HUMAN EFFECTIVENESS DIRECTORATE  
DIRECTED ENERGY BIOEFFECTS DIVISION  
OPTICAL RADIATION BRANCH  
2650 LOUIS BAUER DRIVE  
Brooks AFB, Texas 78235-5105**

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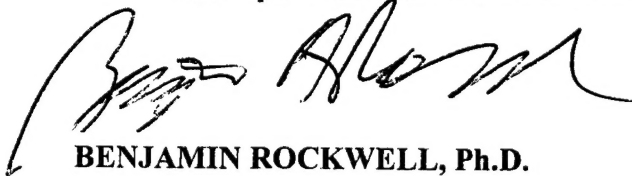
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**BENJAMIN ROCKWELL, Ph.D.**  
Contract Monitor



**RICHARD MILLER, Ph.D.**  
Chief, Directed Energy Bioeffects Division



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## INTRODUCTION

Applications of ultrashort pulse laser systems have increased dramatically in the past several years. Retinal exposure to these laser pulses can produce visible lesions with pulse energies of less than 1 microjoule ( $\mu\text{J}$ ) per pulse. Our research has found a reduction in the energy required for retinal damage as pulse duration is decreased from the nanosecond (ns) to femtosecond (fs) regime. With this data, new laser safety standards are being proposed to reduce the dangers and uncertainties when working around these lasers. [1]

In this technical report we summarize the results and catalog the data of our studies using near infrared laser pulses from several ultrashort pulse laser systems to measure the visible lesion thresholds for several pulse widths for single pulses as well as repetitive pulses from 10 to 10,000 pulses. Also included are results from mode-locked and CW results for the purposes of comparison and base-lining studies. In addition, thresholds were measured for various retinal image sizes from minimal ( $\sim 30\ \mu\text{m}$ ) to almost 1 mm in diameter and thresholds were measured in both macular and paramacular regions within the eye. Minimum Visible Lesion (MVL) thresholds using near-IR wavelengths (1064, 1060 & 800 nm) within the retina of primate (*Macaca Mulatta*) eyes are included in this technical report for femtosecond, picosecond (ps), and nanosecond (ns) laser pulses. Also, one new visible wavelength threshold: 530 nm at a pulse width of 100 fs, (frequency-doubled 1060 nm) was measured. The 50 percent probability ( $\text{ED}_{50}$ ) for damage dosages are reported along with their fiducial limits and probit slopes for both one-hour and 24-hour post-exposures at the 95 percent confidence level. Fluorescein angiography for lesions visible in photographs (FAVL) were accomplished at both the one-hour and 24-hour post-exposure readings.

In a previous report, [2] we summarized the retinal damage thresholds arising from single ultrashort laser pulses of visible wavelengths and compared these with other reported threshold measurements. In this report we are cataloging retinal damage thresholds for single as well as multiple laser pulses of near-infrared wavelengths (and one visible wavelength) and we compare our results with those for both near-infrared and visible wavelengths previously reported.[2]

We report the threshold dosages from near-infrared for ophthalmoscopically visible lesions and the fluorescein angiography threshold dosages for pulse widths of 150 femtoseconds (fs), 1, 20, and 80 picoseconds (ps) and 7 nanoseconds (ns) at one-hour and 24-hour post exposure. These measurements were all taken within the macular area of the retina and all of the multiple pulse measurements using 800 nm and 130 fs pulse widths for 10, 100, 1000, and 10,000 pulses at a pulse repetition rate of 1000 Hz were taken in the paramacular area within 10 degrees or less from the visual axis. One set of measurements was taken at 800 nm and 130 fs simultaneously in both the macula and paramacula to compare the sensitivity of both areas to the ultrashort laser pulses and be able to translate the paramacula thresholds for multiple pulses to the macula area. We also give the results from the comparison of paramacular MVL thresholds from an 800-nm CW source to those produced by a mode-locked source (76MHz, 120 fs) with identical beam propagation characteristics.

## EXPERIMENTAL METHODS

### Laser Systems

Four laser system configurations were required to produce the 5 pulse widths from nanoseconds down to femtoseconds and the repetitive pulses at a repetition rate of 1000 Hz. The 3 longer pulse widths were from one system with a wavelength of 1064 nm while the shortest pulse widths, 100-150 fs and 1 ps were from a second system operating at 800 nm or 1060 nm. We designate the three systems as Laser System I, II, III or IV.

#### Laser System I

Laser System I consisted of a Spectra Physics Model 3800 mode-locked Neodymium:Yttrium-Aluminum-Garnet (Nd:YAG) laser and a Spectra Physics Model GCR-3RA Nd:YAG regenerative amplifier.[3] The long pulses (7 ns) were obtained by operating the regenerative amplifier as a standard Q-switched Nd:YAG laser. The 80 ps pulses were generated by injection seeding the regenerative amplifier with a modelocked pulse from the 3800. The shorter pulses of 20 ps were generated by injection seeding the regenerative amplifier with 5 ps compressed pulses from the mode-locked Nd:YAG. Energies up to several millijoules (mJ) were available for all pulse widths and the beam divergence was  $\sim 0.5$  milliradians. The pulse widths were measured with a fast photodiode for 7 ns pulses and with a slow scan autocorrelator or streak camera for the 20 and 80 ps pulses.

The incident laser beam from System I was apertured to a diameter of 2.5 mm at one-meter distance from the cornea in order to provide a uniform spatial profile for delivery to the corneal surface. This beam was delivered to the eye by deflecting it from a 1064-nm quartz beam splitter mounted on a Zeiss fundus camera. The beam splitter was adjusted such that the deflected beam was collinear with the optical axis of the fundus camera. A low power helium-neon laser was aligned collinear to the incident laser beam for location of retinal exposure sites. The 82-MHz, mode-locked Nd:YAG beam was pulse-compressed to 5 ps and frequency-doubled. In some instances, the 82-MHz mode-locked beam was used to provide marker lesions within the fundus around the macula.

#### Laser System II

Laser System II was a Ti:Sapphire regenerative amplifier system.[4] This system consisted of four major components. The first two of these components were a Coherent MIRA900 Ti:Sapphire oscillator and its pump laser (Coherent INNOVA 200). The oscillator operated at 1060 nm with pulse width of approximately 100 fs. The repetition rate of this oscillator was 76 MHz. This oscillator seeded the regenerative amplifier, a Spectra Physics TSA-1 System. The regenerative amplifier amplified the seed pulse to sufficient energy to provide a large range of energies for this experiment at 130 fs. The regenerative amplifier was pumped by a Spectra Physics GCR-130 Nd:YAG laser with a maximum pulse repetition



frequency of 10 Hz. In all cases the laser system was operated in the single shot mode. The output pulse width of the system was monitored with a slow-scan or single-shot autocorrelator. The marker lesions for this experiment were produced with a Coherent INNOVA 100 CW Krypton gas laser operating at 647 nm. The Krypton laser was shuttered to yield a 3 to 4-ms pulse and the output was adjusted to give a high-contrast, white marker lesion.

In this experimental configuration, illustrated in Figure 2, the eye was positioned so that the retina was in the focal plane of the fundus camera. A beam splitter was placed approximately 1 cm from the cornea and was aligned so the reflected beam entered the eye collinear with the optical axis of the fundus camera. The transmitted portion of the beam was directed to an energy meter. The reflected/transmitted ratio for the beam splitter was measured for each set of exposures. The transmitted energy for each shot was recorded and the measured ratio was applied to obtain the actual energy delivered to the eye.

### Laser System III

The third system, Laser System III, was a modification of System II since it used the same seed source, the Mira 900, but used an upgraded regenerative amplifier pump source (Positive Light Merlin Nd:YLF) and a modified TSA-1 regenerative amplifier operating at 800 nm. It was necessary to pump the Regenerative Amplifier at a 1-KHz rate to give the output at this same rate. With the exception of the 1-KHz pulse repetition frequency, the experimental layout was essentially the same as that for Laser System II. The differing components are shown in Figure 2.

### Laser System IV

The final laser system, Laser System IV, was used in data collection of mode-locked and CW data at 800 nm. This experimental configuration is illustrated in Figure 3. The laser system operated with a mode-locked Coherent MIRA-900 Ti:Sapphire oscillator (with a Coherent INNOVA-200 pump source) operating at 76 MHz, 800 nm, and a pulse width of approximately 100 fs. Spectral bandwidths and pulse widths were always monitored with a spectrometer and autocorrelator while tuning the Ti:Sapphire laser for minimum pulse width and verified by a slow scan autocorrelator. The laser was converted to CW operation by opening the slits required for kerr lens mode-locking and confirmed by observation with a fast (< 300ps rise time) photodiode and digital oscilloscope.

The Ti:Sapphire output was spatially filtered in both CW and mode-locked configurations. Laser beam divergence and beam diameter at the range of the eye were monitored and recorded at each change of configuration. A laser profiler with CCD camera was used to monitor these beam parameters. This ensured that both types of exposures were performed with equivalent parameters.

For this system, the cornea was positioned approximately 1 cm from the final beamsplitter so that the reflected portion of the beam entered the eye. The retina was in the focal plane of the fundus camera and the transmitted portion of the beam was directed to a photodiode so that the exposure duration could be recorded.

Prior to subject placement, the ratio of power delivered to the eye to the amount measured at the monitor detector at the beam splitter marked BS1 (see Figure 3) was recorded. This ratio was verified not to change as a function of power delivered. The ratio was also verified to be equivalent for mode-locked and CW exposures. The ratio of the reflected and transmitted portions of the beam were measured for each day's exposure and recorded. Average power and ratios were measured with a Laser Precision Model RM6600 power meter/ratiometer with RKP-575 detectors.

#### Equipment Notes

All equipment used in these studies was maintained by AFRL/HEDO, and was regularly calibrated according to manufacturer specifications. All power and energy measurement equipment was calibrated to NIST-traceable standards during the period of performance of these experiments.

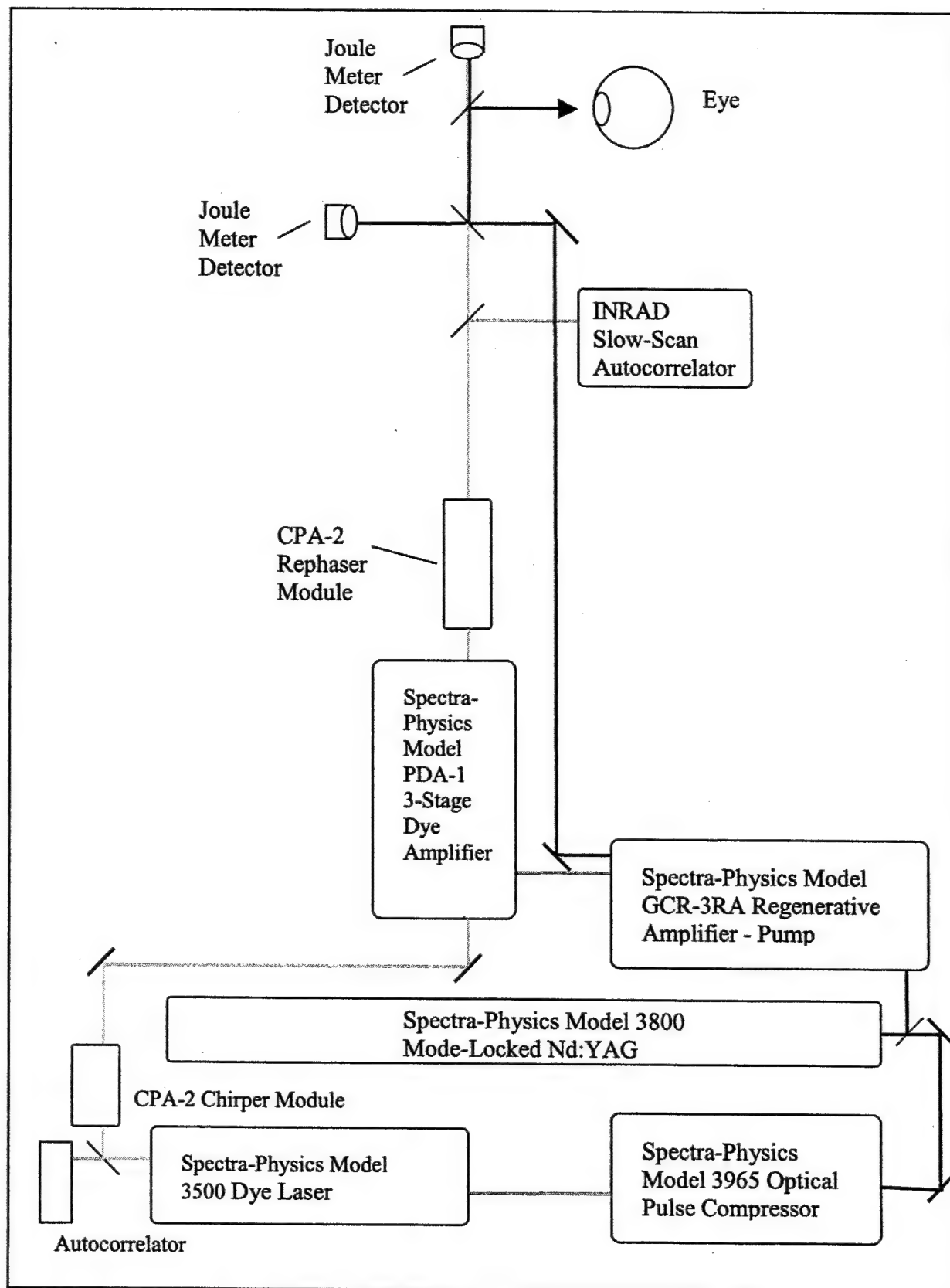
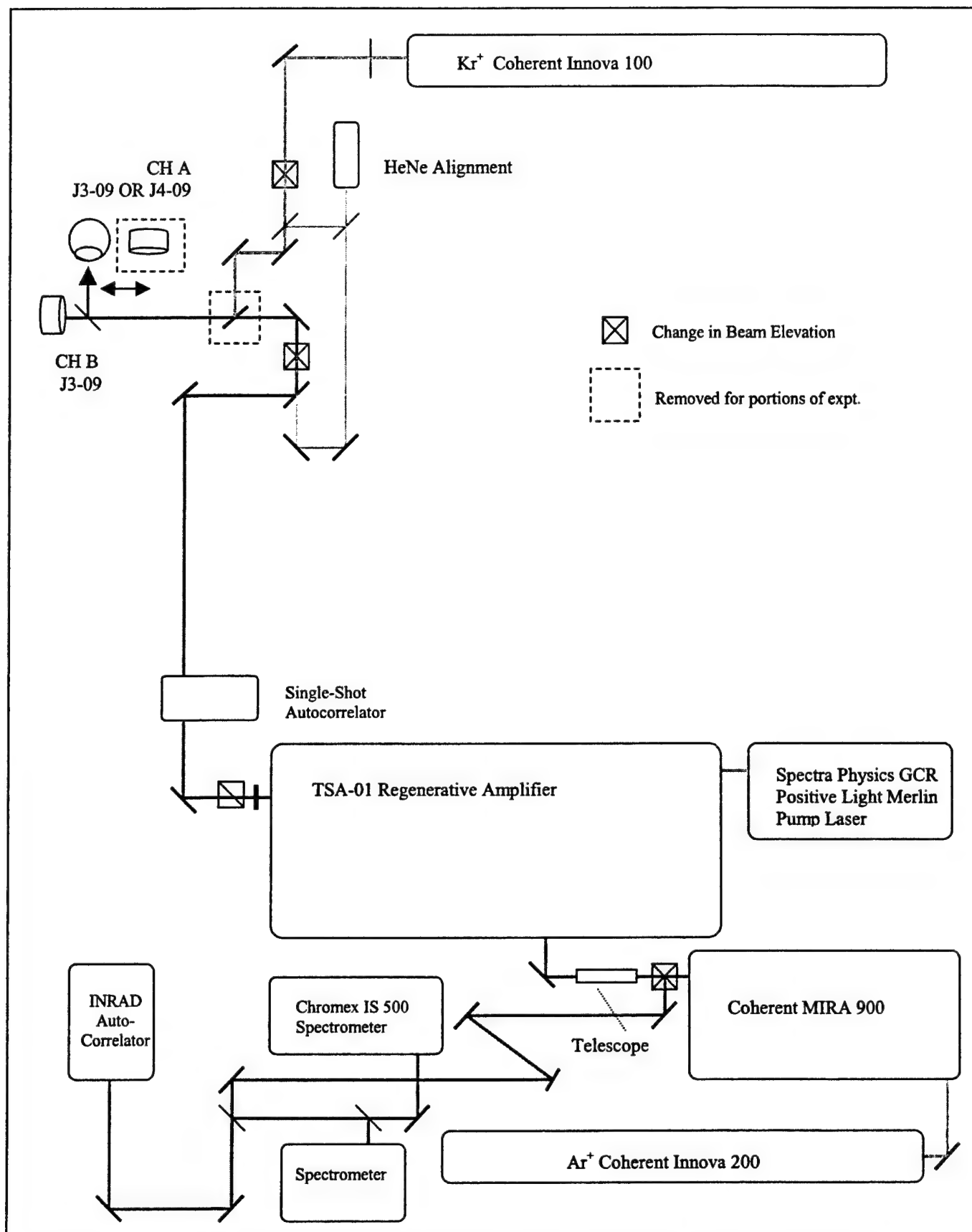


Figure 1. Laser System I Experimental Configuration.



**Figure 2.** Experimental Configuration for Laser Systems II and III, used for 100-fs, 1060-nm and 530-nm data collection.

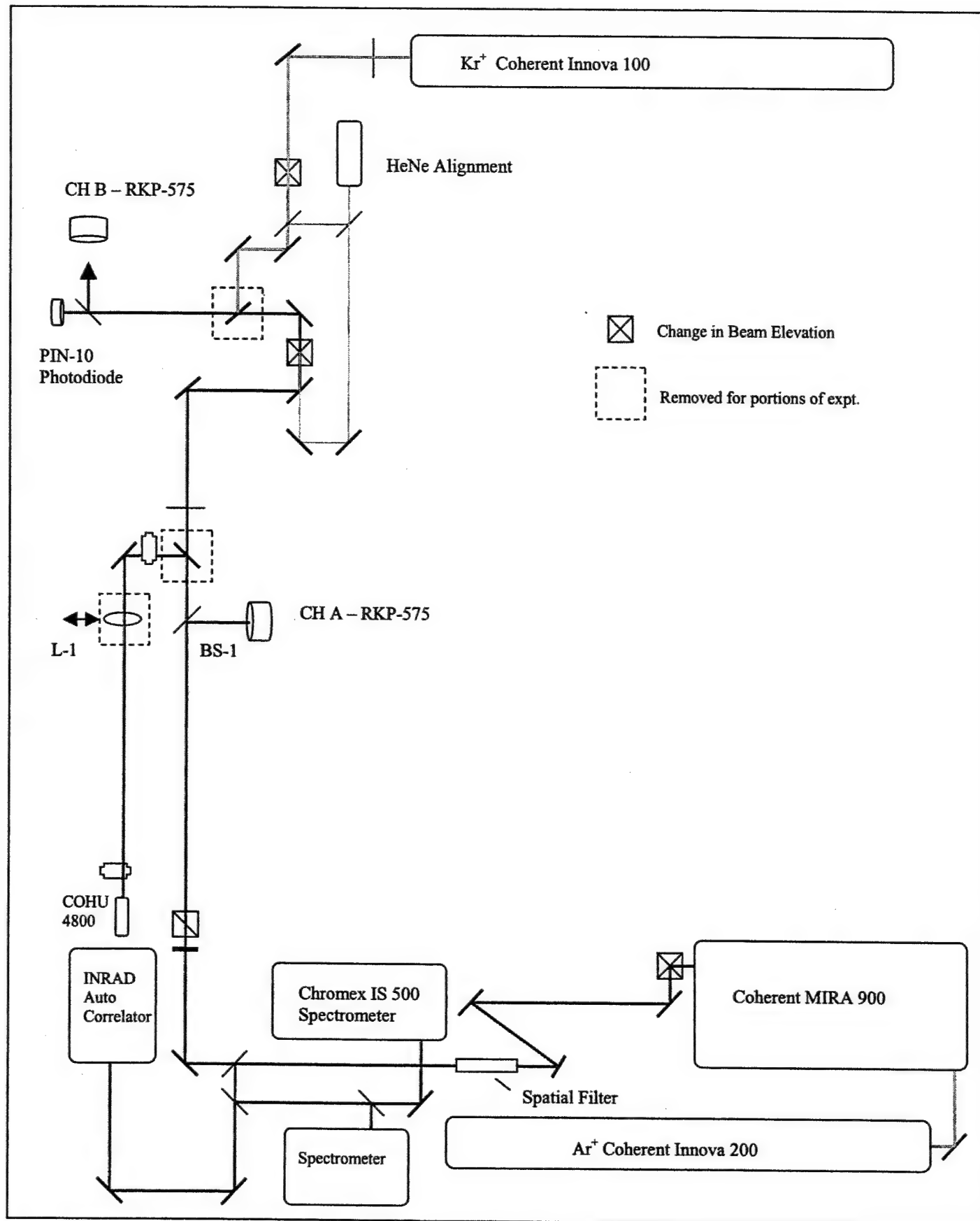


Figure 3. Laser System IV, Experimental Configuration for the Mode-Locked and CW MVL Experiments.

### *In Vivo Models*

Mature *Macaca mulatta* from 2.2 to 6.9 kilograms (kg) were maintained under standard laboratory conditions (12 hours light, 12 hours dark). All primates were screened pre-exposure to ensure that no eye was more than one-half diopter from being emmetropic. All procedures were performed during the light cycle.

### *In Vivo Preparation*

All animals were chemically restrained using 10 milligrams (mg)/kg ketamine hydrochloride (HCl) intramuscularly. Once restrained, 0.16 mg atropine sulfate was administered subcutaneously. Two drops of proparacaine HCl 0.5 percent, phenylephrine HCl 2.5 percent, and tropicamide 1 percent were each administered to both eyes. Under ketamine restraint, the primate had intravenous catheters placed for administration of warmed lactated Ringers solution [10 milliliters (ml)/kg/hour (hr) flow rate] and for administration of propofol. An initial induction dose of propofol (5 mg/kg) was administered to effect. The state of anesthesia was maintained in the monkey using 0.2 - 0.5 mg/kg/min of propofol via syringe pump. The animal was intubated with a cuffed endotracheal tube. A peribulbar injection of 2 percent lidocaine was administered to reduce extraocular muscular movement. The monkey was securely restrained in a prone position on an adjustable stage for fundus photography, laser exposure, and fluorescein angiography (FA). Prior to FA, 0.6 ml of Fluorescein 10 percent (Alcon Laboratories) was administered intravenously. The subject's blood pressure, temperature, and pulse were continuously monitored throughout the experimental protocol. Normal body temperature was maintained by the use of circulating warm water blankets.

The eyelids were held open with a wire lid speculum and the cornea was moistened throughout the procedures with 0.9 percent saline solution. The retina was viewed with a modified fundus camera at all times and all macular exposures (15 to 30) were delivered to the eye, without any external lens system, in a rectangular grid pattern in the macular region of the fundus. Immediately visible retinal marker lesions (created by shuttered exposures of the mode-locked, doubled, compressed Nd:YAG output at 82 Mhz for the three longer pulse widths and a 3-millisecond shuttered exposure of 3 watts of Krypton laser output for the 1 ps and 150 fs pulses) were made in an L-shaped grid pattern of columns and rows to aid in localizing the exposure sites. Fundus photography (including FA) and observation of lesion formation by the researchers were performed with monocular viewing through a Zeiss (or Topcon camera) fundus camera's optical system. Photographs of the fundus were taken immediately before the dye injection, during fluorescein angiography, and continued at intervals of a few seconds until 5 minutes had elapsed, thus providing a sequence of photographs for the development of fluorescein leakage. After fluorescein injection and angiography the lesions were also assessed for fluorescence by viewing through the camera system with excitation and a barrier filter in place. However, fluorescein leakage for the smaller lesions could not be identified by direct observation through the fundus camera and no results using this technique are reported.

A minimum of two examiners evaluated all eyes at one-hour and 24-hour post-exposure. Visible lesions at a given exposure site were reported as a yes only if both examiners identified a lesion. Color fundus photographs were taken at one-hour and 24-hour post-exposure along with black and white photographs of the FA.

### **Statistical Analysis of Data**

The Probit procedure [5], [6] was used to estimate the  $ED_{50}$  dose for creating an MVL in the retina for all pulse widths and to estimate the 95 percent confidence intervals for the  $ED_{50}$  values. Enough data was taken to ensure that the fiducial limits were reasonable and within the following limits at the 24-hour post-exposure reading for visible lesions only. The upper fiducial limit could be no larger than 50 percent greater than the  $ED_{50}$  dosage and the lower fiducial limit could be no less than 50 percent of the  $ED_{50}$  dosage. An experimental goal of a slope of two or greater at the 24-hour observation time was achieved in all cases. The above procedures were used for both ophthalmoscopically visible lesions and fluorescein angiogram data at one-hour and 24-hour post-exposures.

## RESULTS AND ANALYSIS

The results presented in this section consist of five data sets (A – E) that have been thoroughly analyzed and published in peer-reviewed journals. Table 1 summarizes the contents of each data set and literature citations. We have included an overview of each of the five experiments to summarize objectives.

Data Set	Pulse Width & Wavelength	Purpose of Study	Reference
A	7 ns, 1064 nm 80 ps, 1064 nm 1 ps, 1060 nm 150 fs, 1060 nm 150 fs, 530 nm	Single-pulse MVL threshold measurement for the near infrared and one pulse duration in the visible.	[7]
B	150 fs, 1060 nm	Retinal image size dependence of MVL thresholds	[8]
C	150 fs, 800 nm	Macular – paramacular MVL threshold comparison	[9]
D	150 fs, 800 nm	1-KHz multiple-pulse threshold study	[10]
E	CW, 800 nm 150 fs, 800 nm (mode-locked)	Comparison of MVL thresholds for CW and mode-locked fs lasers	[11]

**Table 1.** Summary of the Contents of Data Sets A – E.

### Data Set A: Single-Pulse Damage Thresholds

#### Experimental Overview

In a previous study [2] we reported the retinal damage thresholds arising from single ultrashort laser pulses of *visible* wavelengths. In this study we are reporting retinal damage thresholds for single laser pulses of near-infrared wavelengths and comparing our results with those for both near-infrared and visible wavelengths previously reported.[12], [13], [14], [15], [16], [17], [18], [19], [20], [21], [22], [23]

We have determined the threshold dosages for ophthalmoscopically minimal visible lesions (MVL-ED<sub>50</sub>) for pulse widths of 150 femtoseconds (fs), 1, 20, and 80 picoseconds (ps) and 7 nanoseconds (ns) and the fluorescein angiography threshold dosages at one-hour and 24-hours post exposure. We have previously reported retinal injury studies of visible wavelengths for pulse widths down to 90 fs for pigmented rabbit eyes [24], [25] and for rhesus monkey eyes. [12], [2]



## Minimal Visible Lesion Thresholds

Visible lesion threshold data for all 5 pulse widths are listed in Table 2, for both one-hour and 24-hour post exposures along with the slopes of the probit curves for the 24-hour readings. These slopes were calculated using the SAS probit [5] computer program. The threshold dosages at 24-hour post exposure were lower than for the one-hour reading at all pulse widths. Also, Table 2 lists the number of subjects, eyes used and the number of exposures counted in the probit analysis. Either the right or left eye was selected randomly and depending on availability.

Pulse Width & Wavelength	1-hr Reading MVL-ED <sub>50</sub> (μJ)	24-hr Reading MVL-ED <sub>50</sub> (μJ)	Slope of Probit Curve (24-hr Data)
7 ns, 1064 nm 3 Subjects, 3 Eyes, 69 Expos.	28.7 (22.3 - 39.3)	19.1 (13.6-24.4)	3.3
80 ps, 1064 nm 5 Subjects, 5 Eyes, 100 Expos.	8.1 (5.1 - 16.0)	4.2 (3.0 - 5.8)	2.2
20 ps, 1064 nm 3 Subjects, 3 Eyes, 72 Expos.	5.6 (4.6 - 6.9)	4.6 (3.8 - 5.5)	6.7
1 ps, 1060 nm 2 Subjects, 3 Eyes, 72 Expos.	3.8 (3.0 - 5.6)	2.0 (1.4 - 2.5)	3.2
150 fs, 1060 nm 4 Subjects, 4 Eyes, 81 Expos.	1.8 (1.2 - 2.7)	1.0 (0.8 - 1.2)	4.4
100 fs, 530nm 2 Subjects, 4 Eyes, 63 Expos.	0.36 (0.22 - 0.63)	0.16 (0.11 - 0.23)	3.0

**Table 2.** Minimum visible lesion thresholds for 1064-nm and 532-nm wavelength ED<sub>50</sub> with fiducial limits at the 95 percent confidence level (fiducial limits are in parentheses: fs = femtoseconds, ns = nanoseconds, ps = picoseconds)

Under direct ophthalmoscopic observations, the retinal response to minimal exposures was visible as a pale gray to white lesion increasing in whiteness and in size as energy increased in all exposures as shown in Figure 4. This photograph of the fundus shows the marker grid pattern for 16 exposures within the macular area. Lesions are clearly shown to increase in size with increasing energy of the laser pulse.

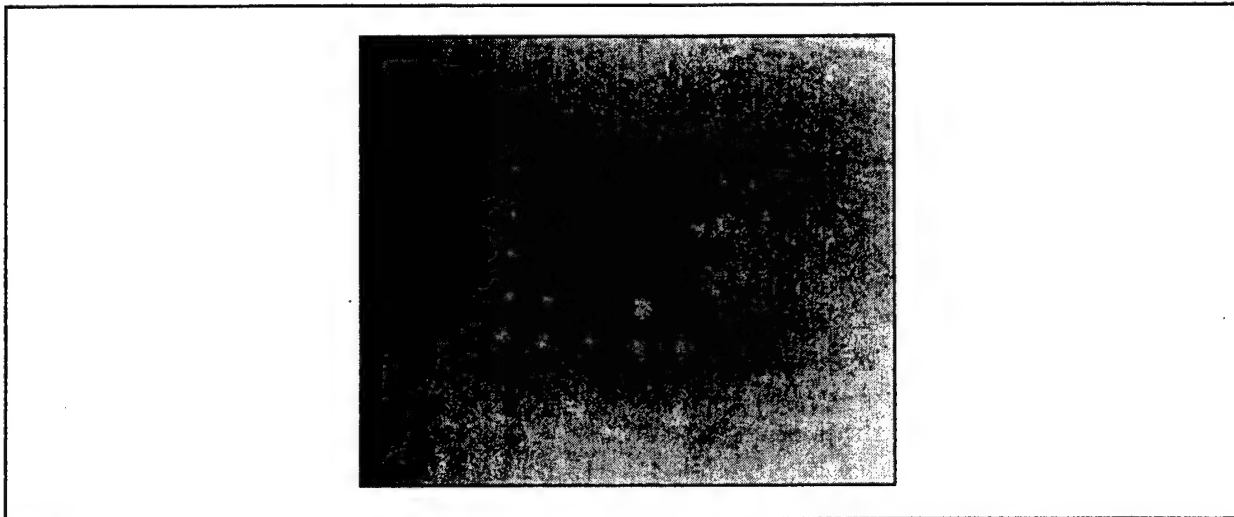
For the 7-nanosecond duration pulses, the number of lesions observable increased with time and there was a 30-percent increase in the number of lesions between the one-hour and 24-hour readings. These additional visible lesions decreased the calculated ED<sub>50</sub> by one-third, from 28.7 μJ at one hour post exposure to 19.1 μJ at 24 hours. The slope of the probit curve was 3.3 for the 24-hour reading and both fiducial limits fell within the range between 1/2 and 1-1/2 times the MVL ED<sub>50</sub> value.

Similar results were recorded for picosecond pulse widths. For 80 ps, the number of visible lesions increased by one-third between the one-hour and 24-hour readings. These

additional visible lesions decreased the calculated  $ED_{50}$  threshold to one-half the value at one hour, from 8.1  $\mu\text{J}$  to 4.2  $\mu\text{J}$ . The slope of the probit curve was greater than 2 and the fiducial limits were reasonable as described above. The number of visible lesions for 20-ps pulse widths did not increase by as large a factor between the one-hour and the 24-hour readings as did the other pulse widths and therefore, there was not as large a difference between the two readings. Also the slope of the probit curve at 24-hour was very large (6.7) as compared with all of our previous measurements.

The above three pulse widths were all generated by the Laser System I and they were obtained from a Nd:YAG laser which was either Q-switched or mode-locked and pulse compressed. The other two pulse widths, 1 ps and 150 fs, were produced by System II, which was a seeded Ti:Sapphire Regenerative amplifier operating at 1060 nm and 530 nm and producing single pulses.

The number of lesions developing within 24 hours versus one hour was almost double for the 1 ps pulse width (42 vs 23). Thus the  $ED_{50}$  at the 24-hour reading (2.0  $\mu\text{J}$ ) was slightly more than 1/2 the  $ED_{50}$  at the one-hour reading (3.8  $\mu\text{J}$ ). The slope of the probit at 24 hours was 3.2, well above the desired value of 2.0 and the fiducial limits for both readings was within the allowed values.



**Figure 4.** Visible lesions in the fundus at 24-hours post exposure for 80-ps, 1064-nm laser pulses. Marker lesions are the column of 5 lesions at the left of the grid and the row of 5 lesions at the lower margin of the grid.

When the pulse width was reduced to 150 fs at 1060 nm, the energy required to produce a visible lesion was also reduced. At the one-hour reading, the  $ED_{50}$  for the threshold was 1.8  $\mu\text{J}$  and that value dropped to 1.0  $\mu\text{J}$  at the 24-hour reading. The actual number of visible lesions at 24 hours increased by 1/3 from the one-hour reading (52 versus 38) and the slope of the probit was large (4.4). Four eyes were used for this pulse width to insure reasonable fiducial limits at the 24-hour reading (both were within  $\pm 20$  percent of  $ED_{50}$ ). Measurements at the doubled 1060 nm of 530 nm were taken as listed in Table 1 and Table 2 at the one-hour reading, the  $ED_{50}$  was smaller by a factor of 5 below the 1060-nm threshold. After 24 hours, the  $ED_{50}$  for the 530

nm was reduced by 6 times and was calculated to be the smallest threshold reported so far (0.16  $\mu\text{J}$ ) for any pulse width or wavelength. At the 24-hour reading, there were almost one and a half times the number of visible lesion at the one-hour reading which reduced the threshold by more than a factor of 50 percent.

### Fluorescein Angiography Thresholds

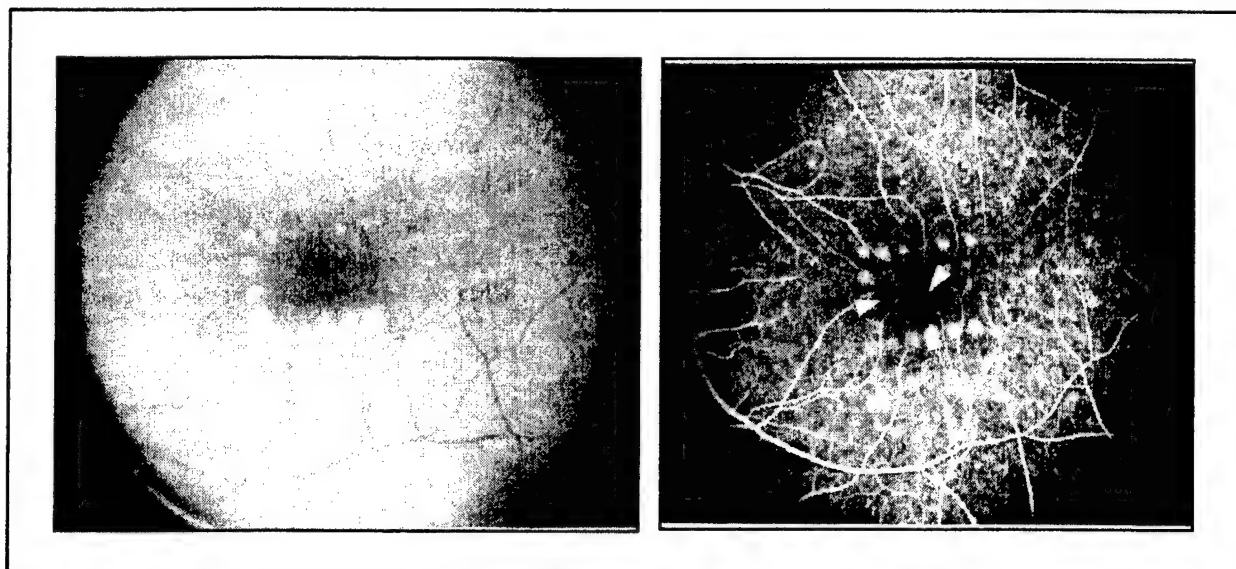
Fluorescein angiographic threshold data for all of the five pulse durations are listed in Table 3, for both one-hour and 24-hour post exposures along with the slopes of the probit curves for the 24-hour readings. Across all pulse widths, the threshold for FA visibility was much higher than the threshold for MVL. Side by side comparison of FAs and fundus photographs demonstrate sites of visible retinal laser lesions without angiographic evidence of damage (Fig 2a & 2b). The threshold for FAVL at one-hour and at 24-hours decreased with pulse width until 1 ps and then increased at 150 fs.

Pulse Width & Wavelength	1-hr Reading FAVL-ED <sub>50</sub> ( $\mu\text{J}$ )	24-hr Reading FAVL-ED <sub>50</sub> ( $\mu\text{J}$ )	Slope of Probit Curve (24-hr Data)
7 ns, 1064 nm	54.4 (41.0 – 87.4)	57.6 (46.5 - 104)	7.7
80 ps, 1064 nm	14.3 (10.8 – 22.0)	14.7 (12.0 - 20.6)	6.0
20 ps, 1064 nm	15.9 (8.6 – 296)	51.4 (no fid.limits)	1.3
1 ps, 1060 nm	6.8 (5.2 - 29.5)	5.15 (4.52 - 6.54)	10.0
150 fs, 1060 nm	15.3 (9.24 – 263)	12.2 (8.77 - none)	5.6

**Table 3.** Fluorescein visible lesion threshold for 1064-nm wavelength ED<sub>50</sub> with fiducial limits at the 95 percent confidence level (fiducial limits are in parentheses: fs = femtoseconds, ns = nanoseconds, ps = picoseconds)

The FA pattern of the test lesions was a fine pale hyperfluorescent spot which appeared within the first 30 seconds of the angiogram and was most prominent in the mid arteriovenous phase or later venous phase of the angiogram. Although many of the lesions, particularly those of higher energy, had persisting or increasing hyperfluorescence in later phases of the angiogram, numerous lesions did not have any persisting hyperfluorescence or leakage beyond the margins of the lesion in late phases. Due to the small size of the laser lesions and the lack of persisting hyperfluorescence later in the angiogram, lower energy laser lesions were quite difficult to differentiate from the normal pattern of choroidal fluorescence. Although the fundus photograph with visible lesions was used as a guide in searching for angiographic lesions, no change in the fluorescein angiogram could be found at the site of many ultrashort pulse laser

retinal lesions that were visible via the fundus camera. The higher energy mode-locked marker lesions demonstrated central hypofluorescence with a ring of hyperfluorescence in early phases of the angiogram, which was most prominent at 24 hours. There was enlargement and blurring of the margins of all marker lesions in late phases of the angiogram causing the lesions to stand out in contrast to the fading fluorescence of the choroidal pattern.



**Figure 5.** (A) Fundus photograph demonstrating the macular grid 24 hours after exposure. Marker lesions extend vertically along the left margin and horizontally across the base of the grid. At the 16 laser sites in the grid, 16 lesions were visible at 24 hours. Three additional unscored test lesions are visible outside the grid. (B) Fluorescein angiogram (FA) image at 24 hours. The marker lesions are visible, as are 13 lesions within the grid. At 3 sites, the laser lesion seen on fundus photograph was not visible on FA (arrowheads).

## Discussion

Retinal thresholds reported for the near-IR wavelengths vary over a broad range depending on the pulse widths and experimental conditions. Most thresholds reported have been in the nanosecond regime, and the threshold for a 20-ns pulse width [17] at 1064 nm has been reported as high as 99  $\mu\text{J}$ . In the picosecond regime, energies reported for the  $\text{ED}_{50\text{s}}$  vary from 2.2  $\mu\text{J}$  at 6 ps to 13  $\mu\text{J}$  at 30 ps for 1064 nm. [16], [19] The lowest retinal threshold reported for near-IR has also been for the shortest pulse width reported (6 ps). [18] Our energies for the 3 pulse widths described above (20 & 80 ps and 7 ns) fall between these limits.

At 7 ns, our 1064-nm threshold, 19  $\mu\text{J}$ , was 21 times the threshold we measured at 4 ns at 532 nm. This value is reasonable since we expected an order in magnitude difference between the two thresholds. However, it is considerably lower than the 99  $\mu\text{J}$  reported by Lund and Beatrice [17] at a pulse width of 20 ns or the 69  $\mu\text{J}$  reported by Ham et al. [18] for 30 ns at 1064 nm. A much larger threshold of 158  $\mu\text{J}$  at the one-hour postexposure reading was reported by Allen, et al [21] for 4-ns pulse widths at 1064 nm. They found no difference between the 1-hr reading and the 24-hr reading whereas our threshold decreased by 1/3 between the one-hour and 24-hour readings (28.7  $\mu\text{J}$  vs 19.1  $\mu\text{J}$ ).

Our measured thresholds at 20 ps and 80 ps of 4.6  $\mu\text{J}$  and 4.2  $\mu\text{J}$ , respectively, are almost exactly an order of magnitude larger than the  $\text{ED}_{50}$  of 0.43  $\mu\text{J}$  for 532-nm exposures at 60 ps. However, both are about double the 2.2  $\mu\text{J}$  at 24 hours reported by Taboada and Gibbons [19] for a pulse width of 6 ps, but they are smaller than the 8.7  $\mu\text{J}$  reported by Goldman et al [13] for a 30-ps pulse width. The thresholds for both pulse widths decreased with time and the fiducial limits were reduced as well. A greater change was recorded for the 80-ps pulse width since the number of visible lesions almost doubled between 1 and 24 hours while there was only a 20 percent increase in the number of visible lesions after 24 hours for the 20-ps pulses. It is not known at this time why there was such a large difference between the thresholds for visible lesions at one hour between the 20-ps and 80-ps pulses while this difference disappeared at the 24-hour reading. Our 1-ps  $\text{ED}_{50}$  of 2.0  $\mu\text{J}$  at 24 hours compares favorably with the 2.2  $\mu\text{J}$  above for the 6 ps pulse width. As with the 80-ps pulse width, the MVL threshold at 1 ps decreased by 1/2 between the one-hour and 24-hour reading. What causes these large decreases in the thresholds cannot be explained at this time and an increased understanding will have to wait for the histology results.

At 150 fs and 1060 nm, our  $\text{ED}_{50}$  of 1.0  $\mu\text{J}$  was recorded at the shortest ever pulse width for near-IR and was the lowest threshold of all our near-IR measurements. However this 1  $\mu\text{J}$  was still 6 times the threshold measured at 530 nm. The difference between the 1060-nm and the 530-nm thresholds for 7 ns was 21 times (19.1 vs 0.90) and for 150-fs the difference was 6 times (1.0 vs 0.16). This 1.0  $\mu\text{J}$  is only slightly more than double the 0.43  $\mu\text{J}$  recorded for the visible wavelength of 580 nm at 90 fs. The number of lesions visible after 24 hours was almost double the number after one hour and hence the  $\text{ED}_{50}$  thresholds decreased by almost one-half at the 24-hour reading. The difference between the one-hour and 24-hour thresholds for the 100-fs and 530-nm pulses was more than a factor of 2 since the threshold decreased from 0.36  $\mu\text{J}$  to 0.16  $\mu\text{J}$ . It is obvious from these data that as the pulse width becomes shorter the wavelength dependence of the thresholds become less. However, the time required for the lesions to develop and become visible increases as the pulse width decreases and does not depend on the wavelength to a great extent.

We did not create a single hemorrhagic lesion with any of the pulse widths during the MVL threshold measurements. This fact was not surprising because Allen et al [21] reported the retinal hemorrhagic threshold for 4-ns, 1064-nm pulses to be 340  $\mu\text{J}$  and our pulse energies for the 7-ns pulse width varied from 8.8  $\mu\text{J}$  to 188  $\mu\text{J}$  within the macula area. Thus we never came close to being near the  $\text{ED}_{50}$  threshold for hemorrhagic lesions. At 80 ps, the pulse energies varied between 1  $\mu\text{J}$  and 54  $\mu\text{J}$  and again, no hemorrhagic lesions. Pulse energies varied between 0.5  $\mu\text{J}$  and 44  $\mu\text{J}$  for the 20-ps pulse widths and from 0.1  $\mu\text{J}$  to 7  $\mu\text{J}$  for pulse width of 1 ps. For the 150-fs pulse width, we varied the pulse energies from less than 0.1  $\mu\text{J}$  to 14  $\mu\text{J}$  without producing a single hemorrhagic lesion. The lack of hemorrhages from 1064-nm ultrashort pulses is in contrast to our previous reports of 532-nm or 580-nm ultrashort pulse laser delivery where intra-retinal hemorrhages were produced by energies as low as two times the MVL  $\text{ED}_{50}$  threshold of 0.43  $\mu\text{J}$ . [2], [12] We will have to wait for the histology before giving any reasons why none were produced.

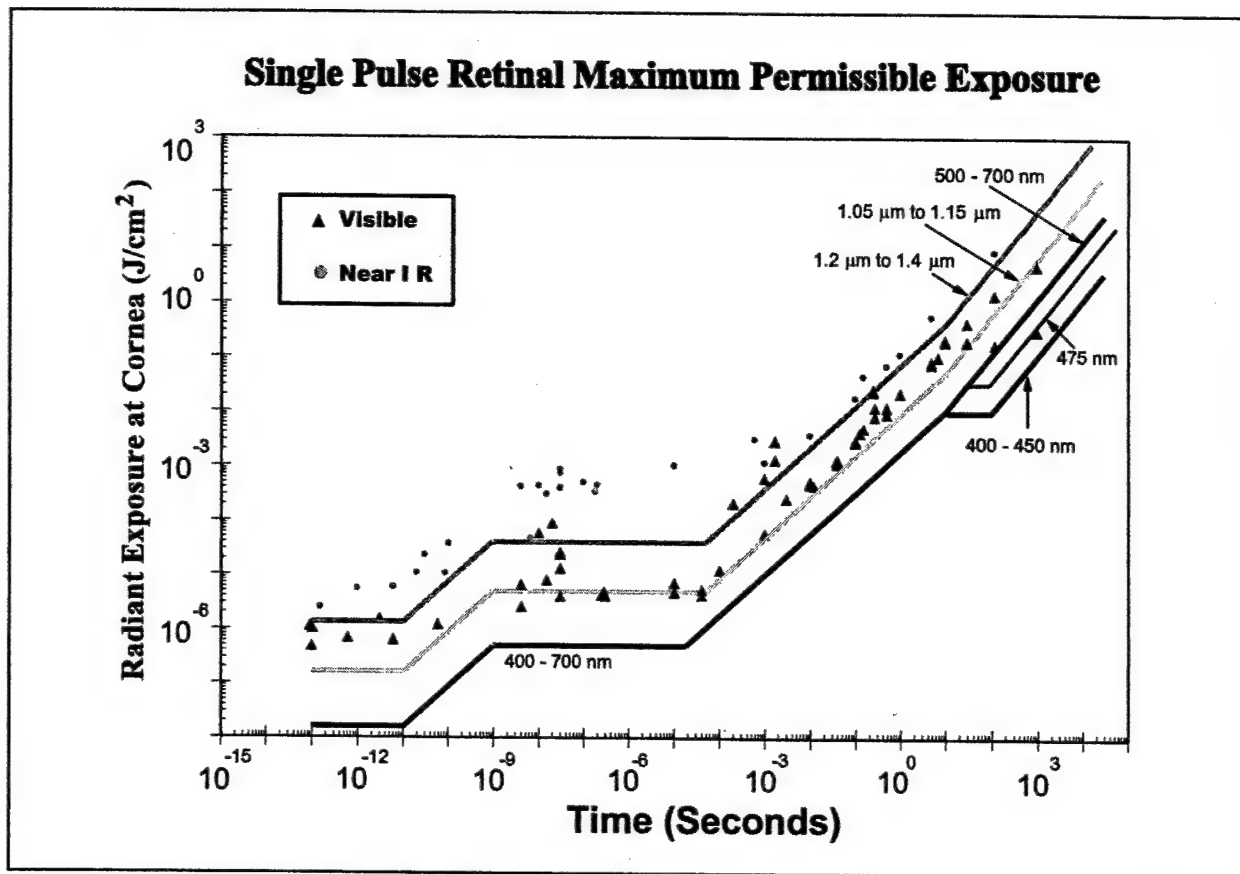


The FAVL findings suggest the retinal laser lesions from pulse energies below the FAVL threshold, do not allow the leakage of fluorescein in a pattern greater than that seen in the normal choroid and retina. In related studies of 532-nm or 580-nm ultrashort pulse laser retinal lesions, Toth et al. [26] found that visible retinal laser lesions with focal RPE damage but without extensive vacuolization did not leak fluorescein dye and Chiu et al [27] demonstrated intact zonula occludentes between laser damaged and adjacent RPE cells. The lower energy 1064-nm ultrashort laser pulses may produce similar RPE injury, which does not break down the barrier function of the RPE.

In Toth et al. [26] and in this study, the MVL lesion size was between 15 and 50  $\mu\text{m}$ . These small lesions, if they do not allow leakage of fluorescein dye, are difficult to differentiate from the background punctate fluorescent pattern of the primate choroid. Borland et al., [20] using a higher concentration of fluorescein dye (20 percent), also noted this problem of "confusion between threshold lesions of small image size and the background of the choroidal flush."

Our FAVL-ED<sub>50</sub> of 58  $\mu\text{J}$  for a 1064-nm, 7-ns pulse, is comparable to the 47  $\mu\text{J}$  FAVL-ED<sub>50</sub> for 1059-nm, 15-ns pulse reported by Borland et al. [20] In contrast, however, we observed visible retinal lesions at much lower energies than reported by Borland et al (MVL-ED<sub>50</sub> of 28.7  $\mu\text{J}$  vs. 135  $\mu\text{J}$ ). The difference in observation of fundus lesions may be due to the method of retinal examination. Borland et al. used a direct ophthalmoscope to examine lesion development at one-hour post exposure, which was subsequently confirmed by studying photographic enlargements of the retinal exposures taken with a fundus camera. In this study, the fundus was observed using a Zeiss or Topcon fundus camera with the observers looking at a magnified image at one and 24-hours post exposure.

Our data using near-IR laser pulses for the rhesus monkey can be compared with other published data as included in the database used to establish the ANSI Z136.1-2000 standard. There are several reported data points for rhesus monkeys for pulse widths <1 ns at near-IR wavelengths as shown in the Figure 6, including Goldman et al, [13] Ham et al, [Ham, 1985 #62] Taboada & Gibbons, [19] Lund & Beatrice. Our data points are shown below all other data points with the exception of the Taboada & Gibbons data for 6 ps. Our data show a definite downward trend from 7 ns to 150 fs for the 24-hour reading. For a decrease in pulse width of 5 orders in magnitude, our MVL- ED<sub>50</sub> thresholds decreased from 19  $\mu\text{J}$  down to 1  $\mu\text{J}$ , or a factor of 20 times. The upper gray line shown in Figure 6 represents the current ANSI Z136.1-2000 retinal maximum permissible exposure for wavelengths between 1.05  $\mu\text{m}$  and 1.15  $\mu\text{m}$  for pulse widths down to 1 ns, which is 5  $\mu\text{J}/\text{cm}^2$ . Thus, 2  $\mu\text{J}$  at the cornea for a pulse width of 1 ns is considered safe; however, one cannot extrapolate this safe level (upper gray line for 1060 nm) to pulse widths below 1 ns. This is because our data include 26 lesions that resulted from pulse energies of less than 2  $\mu\text{J}$  from the total of 94 lesions created for combined pulse widths of 1 ps and 150 fs. Thus the ANSI standard for retinal maximum permissible exposure was revised and extended below 1 ns, with reduced MPE limits, as a result of the research conducted by our group.



**Figure 6.** Retinal maximum permissible exposure from ANSI Z136.1-2000. The solid lines indicate the current national standards below which radiant exposure levels are considered safe. The dots represent the database upon which the safety standard is determined (triangles for laser pulses at visible wavelengths and circles for near-infrared (NIR) wavelengths), and the circled NIR dots are from the present study.

It is important to recognize that although a retinal lesion from low energy ultrashort pulse laser injury may be seen on fundus examination, it will often not be visible on fluorescein angiography. This could make the assessment of a possible mild acute injury more difficult, as a small lesion may be difficult to differentiate from a drusen, and the clinician would typically expect the acute laser lesions to fluoresce. We do not yet know the impact on vision from the presumed minimal focal laser injury to RPE and possibly photoreceptors. With higher energy lesions (above FAVL threshold) this would not be a problem. Unfortunately, at energies close to MVL-ED<sub>50</sub>, and with small retinal lesions, fluorescein leakage may not be evident.

## **Data Set B: Retinal Image Size Dependence**

### **Experimental Overview**

Studies of retinal injury due to laser insult have been reported for decades. Most of these studies have been concerned with measuring the damage thresholds with the eye focusing the laser beam to the smallest retinal spot size possible. A few of these studies, [16], [13], [20], [28], [29], [30], [31] have been performed to measure the effects of larger spot sizes on the retina, simulating the viewing of extended light sources, and having higher damage thresholds. Visible lesion thresholds have been reported for observation times of 5 minutes, one-hour, and 24-hours post exposure. Regardless of the reporting time, the energy required to create a lesion increased with retinal image size. This trend is as expected since the damage mechanism was considered to be thermal in nature. [32], [33]

Pulse width or exposure time is a major factor in creating retinal lesions. For exposure times longer than 10 microseconds, the radiant threshold exposure (in  $\text{J}\cdot\text{cm}^{-2}$ ) at the cornea decreases dramatically with decreasing pulse width. For pulse widths between 10  $\mu\text{s}$  and 1 ns, the radiant exposure at the cornea remains nearly constant for minimal retinal image spot sizes and then decreases in radiant exposure for pulse widths down to 100 fs. [12] In general, it takes less energy to create a visible lesion in the retina as the pulse width is reduced to 100 fs and the radiant exposure at the cornea is likewise reduced. Similarly, the radiant exposure at the retina decreases with decreasing pulse width for minimal retinal image sizes and this radiant exposure (in  $\text{J}\cdot\text{cm}^{-2}$ ) also decreases with increasing retinal image size. This fact first appears as a contradiction, but in reality, the data fits the rate process model as part of the thermal model for retinal lesions.

In the rate process model, as first proposed by Henriques, [32] it is not only the peak temperature rise which causes the damage to the tissue but also the time for which the temperature is increased. Thus it is the temperature-time history that determines damage and not the temperature rise only. This time dependence in the rate process model is precisely what allows the retinal radiant exposure to decrease with increasing retinal image size as reported in the literature. Reductions of more than an order of magnitude in radiant exposure have been measured [28], [20], [13], [29], [30], [31], [34], [35] for increases in retinal image sizes from 20 to 1,000 microns ( $\mu\text{m}$ ). For all exposure durations from 30 ps to 10 seconds, the reported retinal injury thresholds have varied approximately as the reciprocal of the image diameter.

It must be remembered that the energy deposited within the retina increases proportionally with image size at the visible lesion threshold. Additionally, the time required for the elevated temperature within the exposed area to decrease to the body temperature, increases with larger retinal spot sizes. Also note that damage thresholds are reported in several different manners, including energy (in J) entering the eye, radiant exposure at the cornea (in  $\text{J cm}^{-2}$ ) averaged over the pupil area, and radiant exposure at the retina (expressed in  $\text{J cm}^{-2}$ ). [28], [20], [13], [29], [30], [31], [34], [35]



For this experiment, Laser System II was used to generate 150 fs pulses at 1060 nm, with the CW krypton laser beam (647nm) providing a second laser source for creation of retinal marker lesions. A number of optical elements were used to direct the laser beam from the output aperture of the laser to the experimental subjects as shown in Figure 2. The final element of the optical train was a beam splitter used to direct a quantified percentage of the pulse energy to the subject's cornea, which was positioned approximately one centimeter from the beam splitter. The transmitted portion of the beam through the beam splitter was directed to a detector for recording the energy of each pulse. The eye was positioned such that the retina was in the focal plane of a fundus camera used for placement and experimental observation of lesions.

Laser beam diameter at the retina was adjusted through the use of a spherical-concave lens placed 9.5 cm before the cornea. This resulted in a slightly divergent beam entering the eye, creating a focal point location posterior to the plane of the retina, as shown in Figure 7. For the largest retinal beam diameter, 804  $\mu$ m, it was necessary to use a flat-surface contact lens on the cornea along with a +4.5-diopter lens. The beam diameter at the intersection with the retina was computed using a Gaussian beam propagation model. A different lens was used to create each quoted beam diameter. Focal lengths used, along with the computed retinal beam diameters, are listed in Table 4.

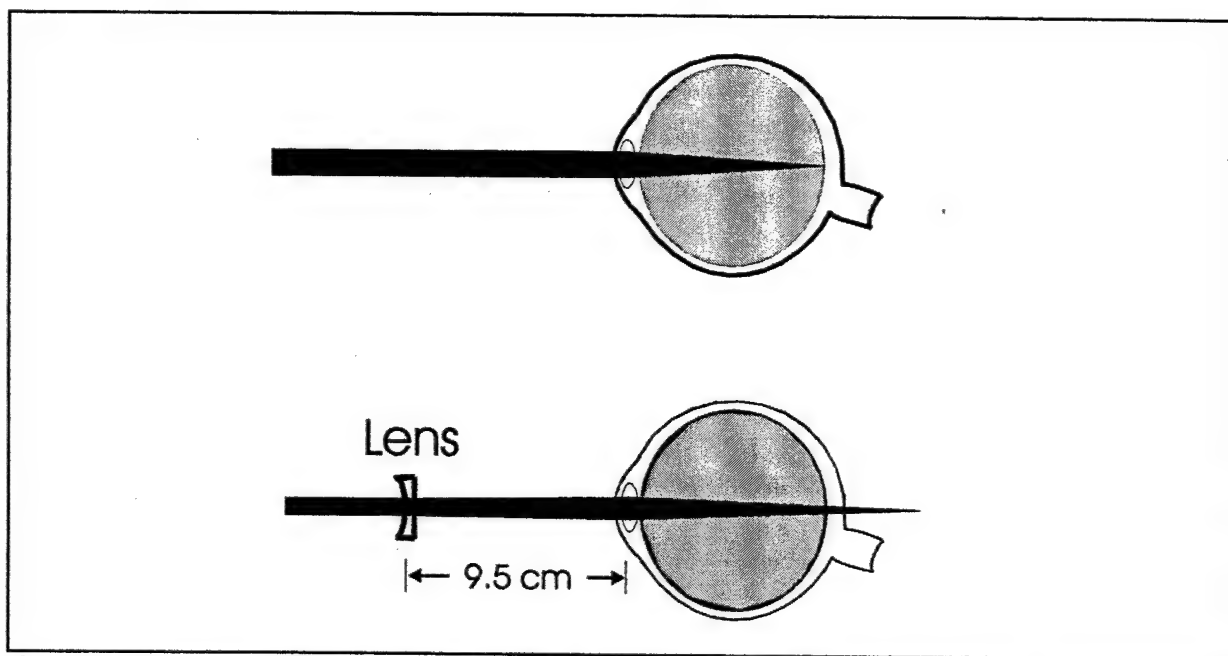


Figure 7: Depiction of the technique used in this study to increase the laser's retinal spot size. Lens focal lengths listed in Table 4 were selected to provide the desired spot diameter.

In all cases, the focal point of the near-IR beam is focused behind the retina and the image diameters are all much larger than for the smallest diameter that can be achieved with visible light. Focusing behind the retina was the simplest method of obtaining the increasing image sizes. For the largest image size, 804  $\mu$ m, it was necessary to use a flat surface contact lens on the cornea as well as a +4.5 diopter lens at a distance of 9.5 cm in front of the eye to

obtain such a large image diameter. We could not use a positive lens with a maxwellian view because of possible laser induced breakdown in air at the focal point before the cornea. With the femtosecond pulse widths, peak powers for the threshold range at the 804  $\mu\text{m}$  diameter were well over 200 MW. Therefore no focal point could be created with the laser beam before or within the eye itself because of nonlinear effects at these peak powers.

Measurements of the minimum visible lesion thresholds for six different retinal image sizes for laser pulses of 150 fs at 1060 nm wavelength are reported. These measurements were made to determine retinal radiant exposure or threshold fluences as the retinal image size was increased from 48  $\mu\text{m}$  to 804  $\mu\text{m}$  in diameter by placing positive and negative lens in front of the eye to change the divergence of the laser beam. Both ophthalmoscopically visible thresholds (MVL) and fluorescein angiography (FA) thresholds were determined.

### Fluorescein Angiography Thresholds

Results for the fluorescein angiography measurements are also listed in Table 4 and thresholds are reported for both the one-hour post exposure and 24-hour post exposure readings. The FA pattern of the test lesions was a fine pale hyperfluorescent spot that appeared within the first 30 seconds of the angiogram. Because of the size, they appeared quite similar to the normal macular fluorescein pattern. In mid and later phases of the angiogram, the lesion increased minimally in fluorescence with very little blurring of the margins of the lesion, in contrast to the blurring leakage from the control marker lesions. This is also in contrast to the late fading of the normal choroidal fluorescein pattern. The test lesions were very large compared to the typical small-spot exposures [7] and no central hypofluorescent area was seen in any of the test lesions either at one-hour or 24-hour. There were no sites of blocked fluorescence as from a retinal or sub-retinal hemorrhage. The higher energy krypton marker lesions demonstrated central hypofluorescence with a ring of hyperfluorescence in the earliest phase of the angiogram with intense hyperfluorescence in midphases. Late leakage demonstrated a blurred hyperfluorescence. In all four larger retinal image diameters, the FA threshold actually increased after 24 hours by a small amount. Thus the one-hour threshold is the more sensitive indicator of damage in these cases.

### Minimal Visible Lesion Thresholds

The results for the ophthalmoscopically visible MVL thresholds are listed in Table 5 for the one-hour and 24-hour post exposure readings. These results clearly show that the thresholds for the ophthalmoscopically visible lesions were much lower after 24 hours than for the one-hour case and in half of the image sizes, the thresholds were less than half the value at one-hour. Fiducial limits were all within the reasonable described in the Experimental Methods section, and the slopes [6] of the probit lines were all greater than 2 at the 24-hour reading as calculated by SAS [5], [36]. Threshold energies for the MVL after 24 hours were the same for the two smallest images even though the calculated image diameters were different by almost a factor of 2. For negative lenses, the threshold energies increased as the image size increased but not proportional to either the image diameter or image area at the retina. For an 11-17 times increase

in the image diameter, the MVL threshold, in microjoules, increased by 54 times at the 24-hour reading while the radiant exposure decreased by a factor of five.

The MVL thresholds listed in Table 5 are all lower than the FAVL thresholds listed in Table 4 with the exceptions of the -5 diopter and -10 diopter lenses at the one-hour readings. In these cases, the FA thresholds actually increased after 24 hours while the MVL thresholds decreased after 24 hours. Otherwise, across all image diameters, the threshold for FA visibility was much higher than the threshold for MVL. In all cases (except the two smaller image diameters) the FAVL thresholds actually increased after 24 hours in contrast to the MVL thresholds which all decreased after 24 hours.

The radiant exposures listed in Table 5 are plotted in Figure 10 as a function of the image diameter on a log scale. Also plotted in this figure are the data points from Beatrice and Frisch [37] to show the general trend for short laser pulses. The trend of decreasing retinal radiance exposure in  $J/cm^2$  for increasing retinal spot sizes has been found for laser pulses from picoseconds to 10-second exposures for different wavelengths. The scaling relationship indicated in this figure is that the retinal injury threshold for these exposure durations varies approximately as the reciprocal of the image diameter for image sizes from 40  $\mu m$  to at least 1 mm. Sliney[35] has gathered a large quantity of published data to show this scaling relationship for retinal image diameters from 20  $\mu m$  to 1 mm.

Focal Length of Lens Used	Focus Behind Retina (mm)	Diameter of Image at Retina ( $\mu m$ )	1-hr Reading FAVL-ED <sub>50</sub> ( $\mu J$ )	24-Hr Reading FAVL-ED <sub>50</sub> ( $\mu J$ )
+0.75 Diopter	0.32	48	No data	No data
None	0.44	70	15.3 (9.2-262)	12.2 (8.8-#)
-1 Diopter	0.60	102	5.5 (3.4-27)	7.4 (5.9-#)
-5 Diopter	0.99	224	10.1 (8-14)	12.1 (10-17)
-10 Diopter	1.30	378	32.1 (26-41)	35.3 (27-58)
+4.5 Diopter w/ Contact Lens	2.8	804	189 (135-279)	205 (145-309)

Table 4. FAVL thresholds for 150 fs, 1060 nm, for different retinal image sizes (Note: Lenses were placed 9.5 cm in front of the eye. Fiducial limits are shown in parentheses. '#' designates no upper fiducial limit provided by probit.)

Image Diameter ( $\mu\text{m}$ )	Image Area ( $\text{cm}^2$ )	1-Hr Reading MVL-ED <sub>50</sub> ( $\mu\text{J}$ )	24-Hr Reading MVL-ED <sub>50</sub> ( $\mu\text{J}$ )	Radiant Exposure ( $\text{J}/\text{cm}^2$ )
48	1.79E-05	2.3 (1.2-10)	1.0 (0.6 - 1.8)	0.056
70	3.93E-05	1.8 (1.2-2.7)	1.0 (0.8 - 1.2)	0.026
102	8.08E-05	3.2 (2.3-4.6)	2.1 (1.3 - 3.0)	0.026
224	39.5E-05	16.6 (9.3-170)	7.2 (5.2 - 9.9)	0.018
378	112E-05	38.1 (28-72)	19.7 (14.7-25)	0.017
804	506E-05	81 (41-142)	54.1 (28-80)	0.011

**Table 5.** MVL thresholds and radiant exposures for 150 fs, 1060 nm, for different retinal image sizes. Fiducial limits are shown in parentheses.

## Discussion

In agreement with our previously reported FA studies, the measured FAVL values show that FA is not a good indicator of minimal retinal damage [7], [12], [38]. There were only 2 measurements for FAVL that gave lower thresholds than the MVL, and those were for the one-hour reading listed in Table 4. In our previous studies it was thought that the small image sizes were the reason for the higher FA thresholds but with these large image sizes, a reevaluation was required through a study of histopathology as discussed below.

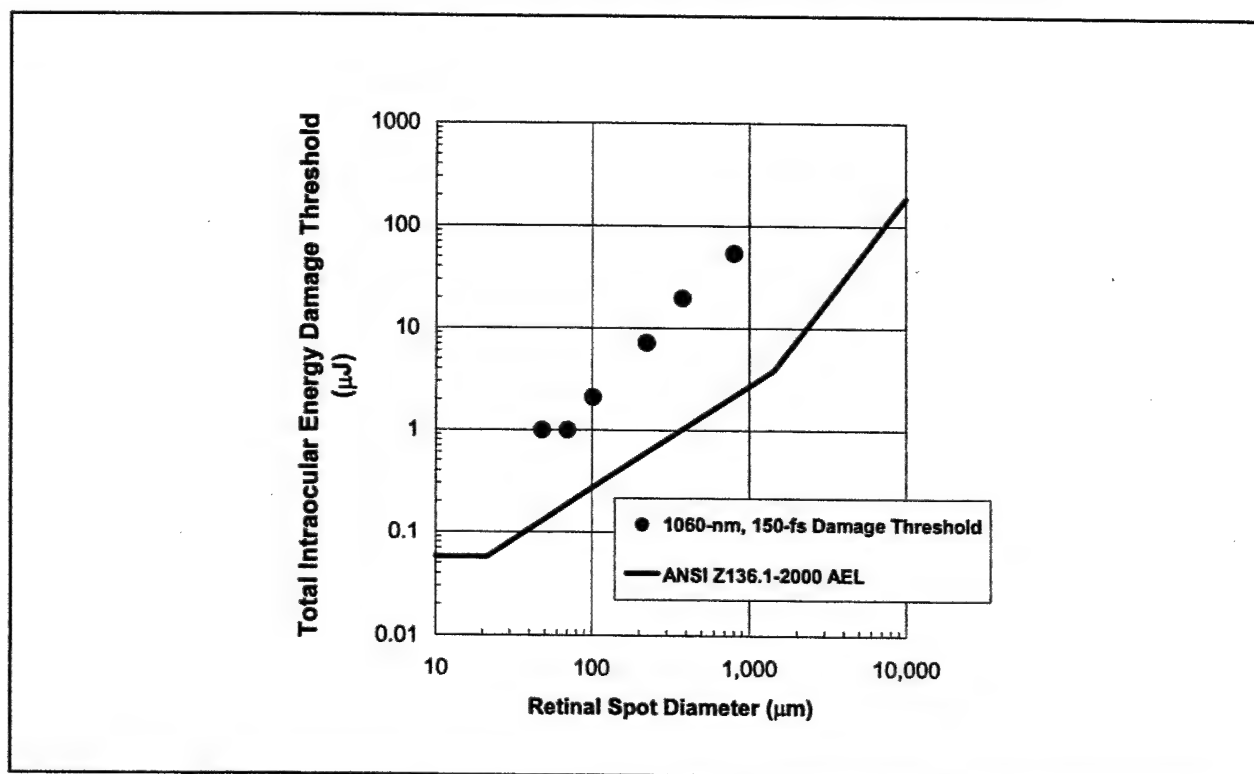
The large-spot laser lesions were remarkable in their clinical and pathological appearance. The lesions, rather than centering on a single focal spot of pallor, as typically seen in pulsed laser lesions of the retina, demonstrated a spotted pattern of multiple focal lesions across the area of laser delivery. Further analysis of retinal histopathology was conducted for several beam diameter values and was reported in detail elsewhere.[39] Atypical focal "scattered shot" lesions were seen for the largest two spot diameters. The histopathology study revealed that after delivery of 7.9 times the ED<sub>50</sub> energy, there was a lack of diffuse spread of damage into the neurosensory retina. Instead, focal photoreceptor injury occurred in sites corresponding presumably to whitened lesions observed on fundus examination. At low energy, areas of punctate RPE injury were scattered across an individual exposure site.

Despite the mild retinal involvement in the laser lesions, there were focal sites of choriocapillaris injury. This was similar to the injury pattern seen in small-spot, near-infrared, ultrashort-pulse laser retinal lesions. These sites were infrequent enough to be difficult to correlate specifically with the focal sites of RPE damage. Histopathology from acute lesions is currently being investigated in order to determine whether there is a correlation.

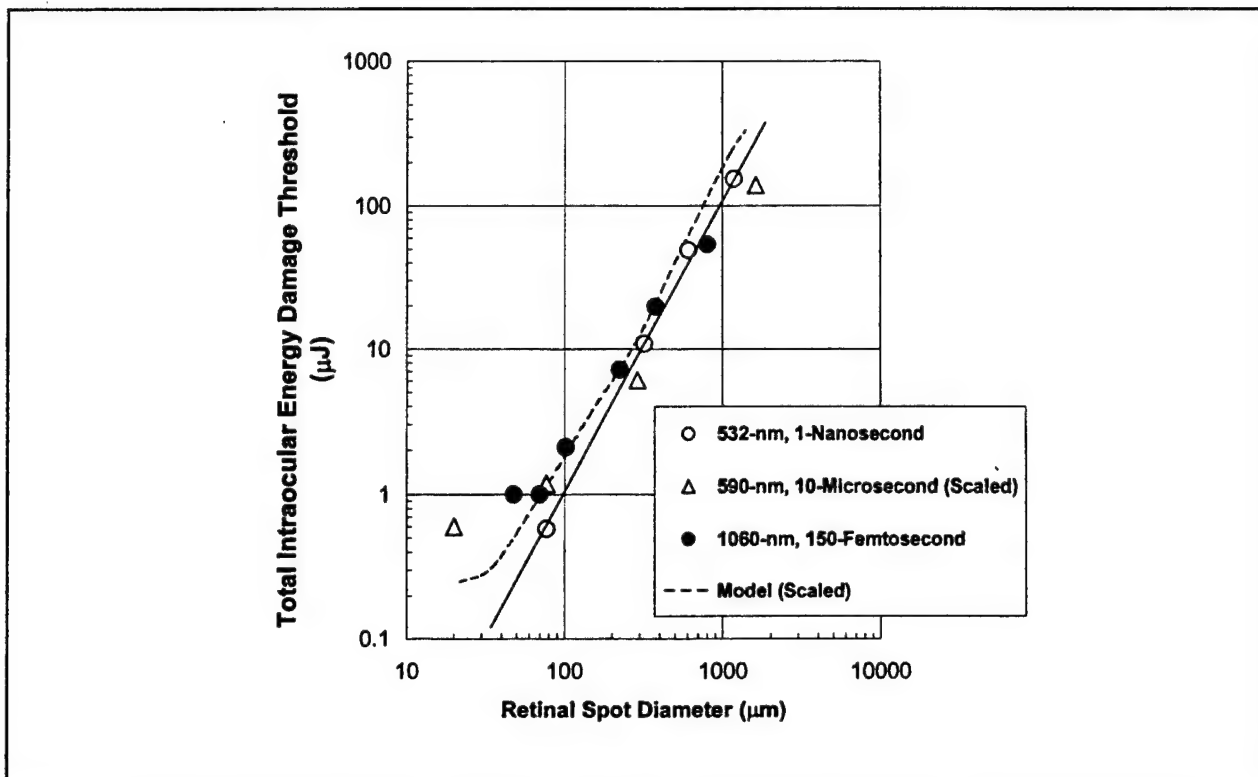
Although we have postulated various aberrations in lenses and laser delivery, it is difficult to explain how such a pattern could be produced. This is particularly interesting since

the threshold for injury for the 804-micron retinal spot is at a lower radiant exposure (in J-cm<sup>-2</sup>) at the retina. One explanation for this effect could be multiple filamentation associated with self-focusing of the broad, high-energy 150-fs beam as it traverses the globe. Previous reports of filamentation patterns in non-biological materials, describe a scattered pattern [40] of focal spots of laser energy a few micrometers in diameter. A filamentation pattern of laser energy might be seen in the RPE, with its thin layer of scattered melanosomes, similar to the distribution of particles in a photographic film emulsion. The focal energy at the sites of filamentation may be adequate to cause focal lesions similar in appearance to the small-spot diameters produced in Shen's report, [40] possibly explaining the similarity in relative detection thresholds through FA and ophthalmoscopic observations. Although the damage mechanism is suspect due to the unusual pathology observed, damage threshold levels as well as trends with laser spot size compare quite well with previous studies, and with established trends for accessible emission limits (AEL) found in the ANSI Z136.1-200 Standard.

Our image diameter increased by a factor of 17, from 48 to 804  $\mu\text{m}$  while the retinal radiant exposure decreased by a factor of 5. This decrease in fluence is smaller than all other data reported for comparable retinal spot size changes from 20 ps to 10 seconds. We suspect other effects, such as nonlinear phenomena, may be influencing our thresholds for the smaller spot sizes, which would also affect the slope of our data trend in Figure 10. The data from Beatrice and Frisch show a larger negative slope than our data but their data is for 30 ns pulses, which makes their thresholds at small spot sizes much larger than our thresholds.



**Figure 8:** The 24-hour ophthalmoscopically visible lesion threshold data as a function of retinal image diameter. The solid line represents the ANSI Z136.1 Standard AEL for 150 fs, 1060 nm laser pulses as a function of retinal image size.



**Figure 9:** Damage threshold data from this study compared to data from Zuclich et al. and theoretical damage threshold models. The solid line represents a slope of two on the log-log plot.

Figure 8 contains a plot of the data obtained from this study along with the current exposure limits from the ANSI Z136.1-2000 Standard, plotted as a solid line. Although the exposure limit for a small source subtending less than 1.5 mrad in the field of vision is based upon available data from a number of collimated laser studies, the exposure limits for extended sources and large extended sources were extrapolated from longer-duration pulse studies.

The current ANSI Z136.1 Standard trend for the 150-fs duration pulse is a constant value of about 58 nanojoules up to the point where the retinal image subtends 1.5 mrad, corresponding to a retinal image size of approximately 22 μm. The exposure limit for larger image sizes from 1.5 mrad to 100 mrad follow a trend of a linear increase (slope of one in the log-log plot). For image diameters greater than 100 mrad, the exposure limit increases as the square of the image diameter. Figure 8 demonstrates that our damage threshold data, with the exception of the smallest image diameter, follow a slope of greater than one, but not quite a slope of two on the log-log plot. All of the data collected in our study are contained within the 1.5 mrad to 100 mrad angle range, and the current ANSI Standard provides a safety factor of as-little-as 5 for the ultrashort pulses of this study. For an extended-source analysis, the ANSI Standard assumes that the minimal retinal spot size will subtend an angle less than 1.5 mrad. Our data and calculations indicate that a collimated beam into a non-accommodated eye will produce a 40-mm diameter retinal spot size because of chromatic aberration at this wavelength. It should be noted that the retinal spot size calculation has uncertainty, especially for the smaller spot sizes, because the



value is derived from a model eye that does not include all aberrations for the anesthetized subjects of this study. Further analysis of this and other data is warranted in the laser safety community to determine the appropriate extended-source evaluation criteria (e.g.  $\alpha_{\min}$  may need to be a function of wavelength).

The nearest comparison of data from similar experimental work is provided by Zuclich *et al.* [31] in which 5-ns, 532-nm laser pulses were employed with varying retinal image diameters. Their study found that for laser spot diameters of greater than 100 microns, the threshold dosage required increases as approximately image diameter squared. For smaller image diameters, their study found that a transition region existed in which the threshold was invariant as a function of retinal spot size, to a point at which the threshold was increasing as a function of diameter squared. Their study also provided data for 10-microsecond, 590-nm laser pulses, which demonstrated similar trends, but with an approximate 20-fold increase in damage threshold consistent across all retinal beam diameters.

Additional data are available from Beatrice and Frisch [28] who collected a limited number of points from 30-ns, 694-nm laser exposures. The study found that the damage threshold increased linearly as a function of image diameter with retinal image diameters from 40  $\mu\text{m}$  to 1000  $\mu\text{m}$ . Data from long pulse duration exposures have been cataloged by Sliney [35] to show scaling relationships for retinal image diameters from 20  $\mu\text{m}$  to 1 mm.

Data from our study and that of Zuclich *et al.* [31] are presented in Figure 9. We note that there is good agreement between the 150-fs data from our study and the 5-ns data presented by Zuclich *et al.* A significantly lower threshold is anticipated for the 150-fs pulses than for a 5-ns pulse at the same wavelength. However, infrared laser exposures with similar pulse widths are expected to have a higher damage threshold than their visible counterparts because of the increased retinal spot size due to chromatic aberration and the reduction in melanin absorption. The two competing trends in retinal damage threshold due to decreasing pulse width and different wavelengths bring the damage thresholds into convenient agreement for comparison. The 590-nm 10- $\mu\text{s}$  data of Zuclich *et al.* are also displayed in Figure 9. The damage threshold for this longer pulse duration is significantly higher than the nanosecond data from the same study. We have scaled the Zuclich microsecond values by a factor of twenty in order to compare the trends in the data. A solid line with a slope of two on the logarithmic plot is presented for comparison to the anticipated trend of damage threshold increasing as a function of retinal beam diameter squared. All three data sets indicate that as image diameter is reduced, the damage threshold decreases as approximately the image diameter squared. The data sets also indicate that at the smallest image diameter the slope decreases.

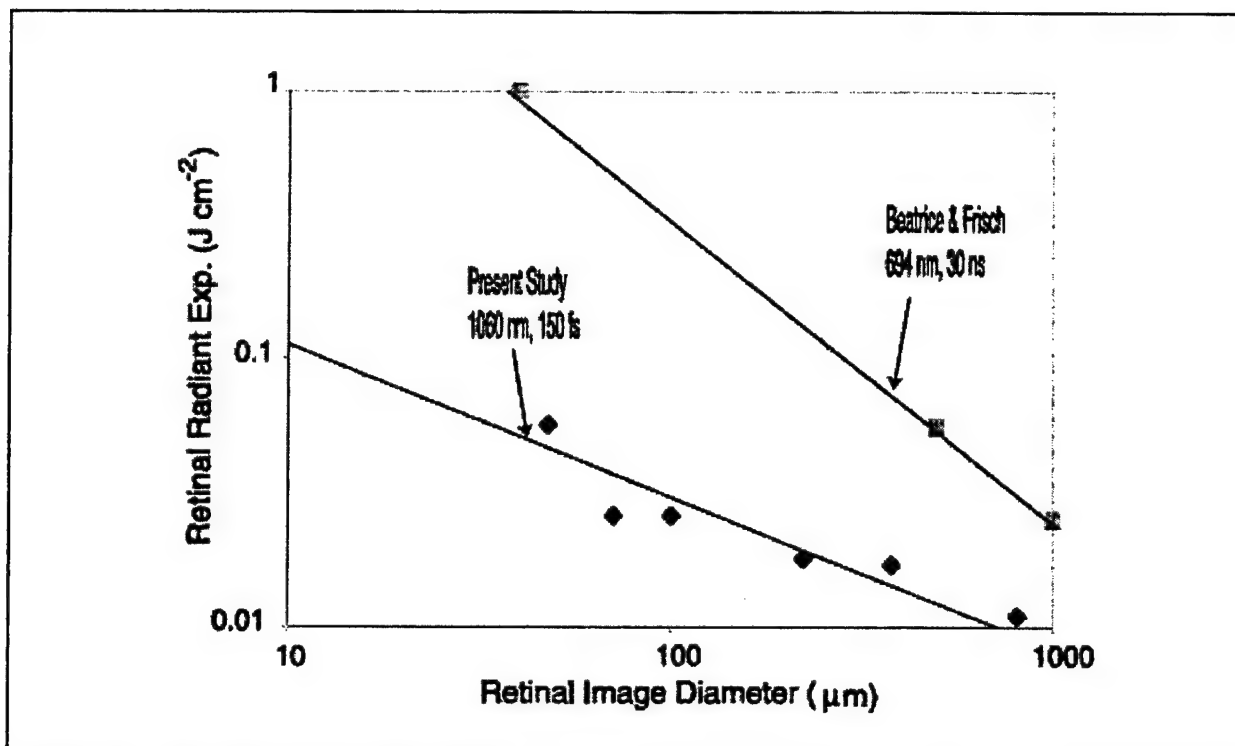


Figure 10. Logarithmic plot of radiant exposures at the MVL-ED<sub>50</sub> vs image diameters (straight lines are shown for visual aid only; they are not calculated from actual values)

Temperature models and measurements [33], [41], [42], [43], [44] which predict the temperature rise in the fundus and the damage thresholds for laser pulses longer than a microsecond have been around for several decades. Most of these models utilize the bulk optical and thermal properties of the eye but are not able to predict damage for very short laser pulses. Other models are being tested which use discrete components of the eye such as melanin granules as the absorbing material and will work for pulse widths below 1 nanosecond (ns).

Temperature models can be very accurate in calculating the temperature rise and damage thresholds for increasing retinal spot sizes from microns to millimeters and do predict the decreasing retinal radiant exposure or fluences for increasing retinal spot sizes. There is little doubt that the damage mechanism for long exposure durations is dependent on the temperature-time history within the tissue and follows the rate process model first proposed by Henriques [32]. However it is not known how short of pulses may be used with this model to predict the damage or if the model is accurate for pulse widths below a nanosecond. The data accumulated by Sliney [35] show the retinal thresholds to vary approximately as the reciprocal of the image diameter for pulse widths as low as 30 ps. Herein we show that a similar relationship holds for pulse widths at 150 fs and that the threshold radiant exposures are much lower for image diameters from 40 μm to 800 μm. The smaller thresholds are to be expected because at the minimum image diameter we have reported some of the lowest MVL threshold for near infrared to date [7].



Included in Figure 9 is a plot of theoretical calculation data from Zuclich *et al.*, [31] employing the Thompson-Gerstman [45], [46] granule retinal damage model. The model is available in our laboratories for comparison to experimental data, given any set of laser parameters. We have scaled the absolute threshold in order to compare damage threshold trends, as the model predicts slightly larger values. Results are independent of pulse duration for short pulses, when the pulse is much shorter than thermal relaxation times in tissue ( $\sim 10 \mu\text{s}$ ). The model produces a good agreement with the trends seen in our data and with those demonstrated in studies by Zuclich. It predicts a flattening in the curve for the smallest retinal image sizes and a slope of slightly less than two on the log-log plot for retinal image sizes between 50 and 300  $\mu\text{m}$  in diameter. For larger retinal image sizes, the damage threshold trend approaches a slope of two. This can be compared with the solid line with slope of two in the graph, provided as a guide to the eye.

In summary, we provide laser damage thresholds for 150-fs, 1060-nm laser pulses as a function of retinal image diameter. Although histopathology indicates a unique damage pattern, the anticipated trends in damage threshold are followed. Comparison with previous studies and theoretical models indicate that these damage threshold trends are predictable, and that the newest guidance provided by the ANSI Z136.1 Standard is appropriate for this ultrashort pulse duration.

### **Data Set C: Macula/Paramacula MVL Thresholds**

#### **Experimental Overview**

Our goal in this study was to evaluate retinal damage thresholds from single ultrashort laser pulses at 800 nm and to compare damage thresholds between macular and paramacular areas within the fundus.[47] Pulse widths of 130 fs were utilized to establish the minimum visible lesion (MVL) thresholds (ED50) within the macula and paramacula. In this study we compare our results with those for both near-IR and visible wavelengths previously reported [12], [15], [16], [14], [17], [13], [19], [7], [18], [20], [48], [49]

Laser-ocular tissue interaction studies for pulse widths below 1 ns are critical to the development of safety standards [50], [51], and in identifying hazards to the human eye from those systems presently operating in the near-IR regime. An understanding of laser-tissue interactions is basic to identifying the potential for injury and to applying therapeutic medical treatments to laser injury and disease. Laser effects in the eye have been well documented for continuous wave and pulsed laser systems with pulse widths down to 90 femtoseconds for visible wavelengths and down to 150 fs [12], [7] for 1060 nm. Thus we are providing the urgently needed data at 800 nm in the primate fundus to recommend new national and international laser safety standards for laser systems operating in the near-IR and to assess potential human retinal hazards from these laser sources.

The retina was viewed with a fundus camera at all times and all macular exposures (16-30) were delivered to the eye in a rectangular grid pattern centered on the fovea. The paramacular exposures (16-30) were placed no more than 10 degrees temporal to the fovea and additional lesions within 5 degrees below (see Figure 11). The right or left eye was selected randomly for exposures. All eyes were evaluated at one and 24-hour post exposure and visible lesions at a given exposure site were reported when at least two examiners identified a lesion. Color fundus photographs were taken at one and 24-hour post exposure along with black-and-white FA photographs.

### Minimal Visible Lesion Thresholds

Results for the macula/paramacula single pulses thresholds are listed in Table 6 for both at the one-hour and 24-hour post exposure readings. Over half of the data points listed were taken using single pulses when the laser system was operating at 10 pps and the rest were taken at a repetition rate of 1000 Hz. Regardless of the repetition rate of the laser system only single shots were delivered to the eye for these experiments. Each repetition rate is listed with its thresholds for both 1-hour and 24-hour readings. Also listed is the combined data for both sets and will be reported as the final thresholds measured.

Location	Mode of Operation	1-hr Reading MVL-ED <sub>50</sub> ( $\mu$ J/pulse)	24-hr Reading MVL-ED <sub>50</sub> ( $\mu$ J/pulse)	Slope of Probit Curve (24-hr Data)
Macula	10 Hz	0.50 (0.32-0.73)	0.38 (0.21-0.57)	2.1
	1 kHz	0.30 (0.21-0.43)	0.26 (0.18-0.38)	3.3
	Combined data 113 shots	0.40 (0.30-0.53)	0.35 (0.26-0.46)	2.4
Paramacula	10 Hz	0.73 (0.50-1.42)	0.55 (0.37-0.84)	2.3
	1 kHz	0.66 (0.47-1.29)	0.56 (0.40-0.89)	2.8
	Combined data 122 shots	0.65 (0.51-0.91)	0.55 (0.44-0.73)	2.5

**Table 6.** Macula/paramacula thresholds at one and 24 hours for single pulses with fiducial limits and slopes of the probit curve.

It is clearly evident that the thresholds decrease from the one-hour reading to the 24-hour reading in all cases. The 24-hour reading is from 5 to 20 percent lower as shown and the thresholds are not significantly different between the two laser systems. The fiducial limits are within the  $\pm 50$  percent limits we have imposed on only the 24-hour readings and the slopes are all greater than 2. Since significantly more data would be required to reduce the fiducial limits at the one-hour reading we determined that this was not practical for this set of experiments. Threshold differences between the macula and paramacula at the 24-hour reading are rather small, 0.55  $\mu$ J for the paramacula and 0.35  $\mu$ J for the macula.

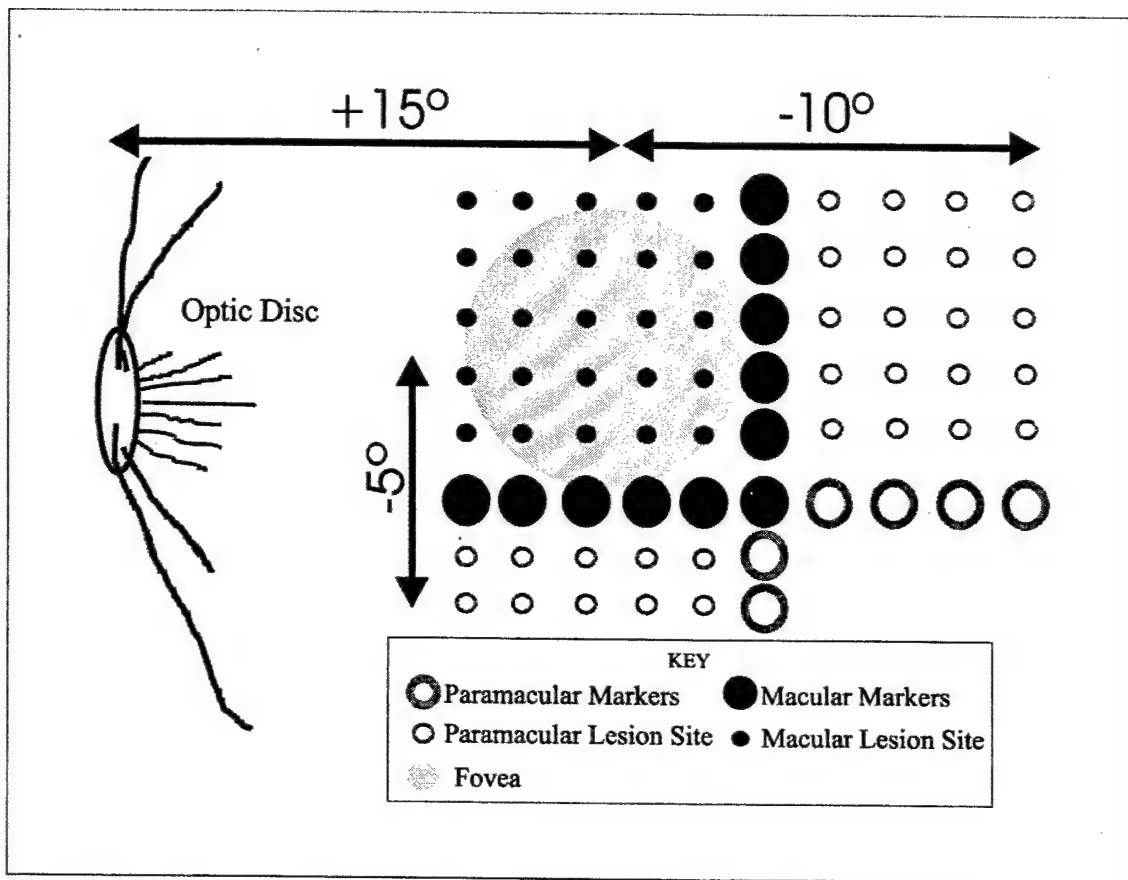


Figure 11: Grid map for lesion placement in macular and paramacular regions of the retina.

## Discussion

In this study we used two different modes of operation for the Ti:Sapphire regenerative amplifier system (See Figure 3). We measured thresholds for both paramacular and macular areas of the retina with both systems. As shown in Table 6 the values were slightly different in the macular area for the two modes of operation. The major difference being that the macular MVL threshold for the 1-kHz mode was slightly lower than that of the 10-Hz mode, while the paramacular MVL thresholds were essentially the same for both modes of operation. When the data for the respective regions were combined and analyzed, a value of 1.6 was obtained for the ratio of paramacular to macular MVL thresholds for these 800-nm, 130-fs, laser pulses.

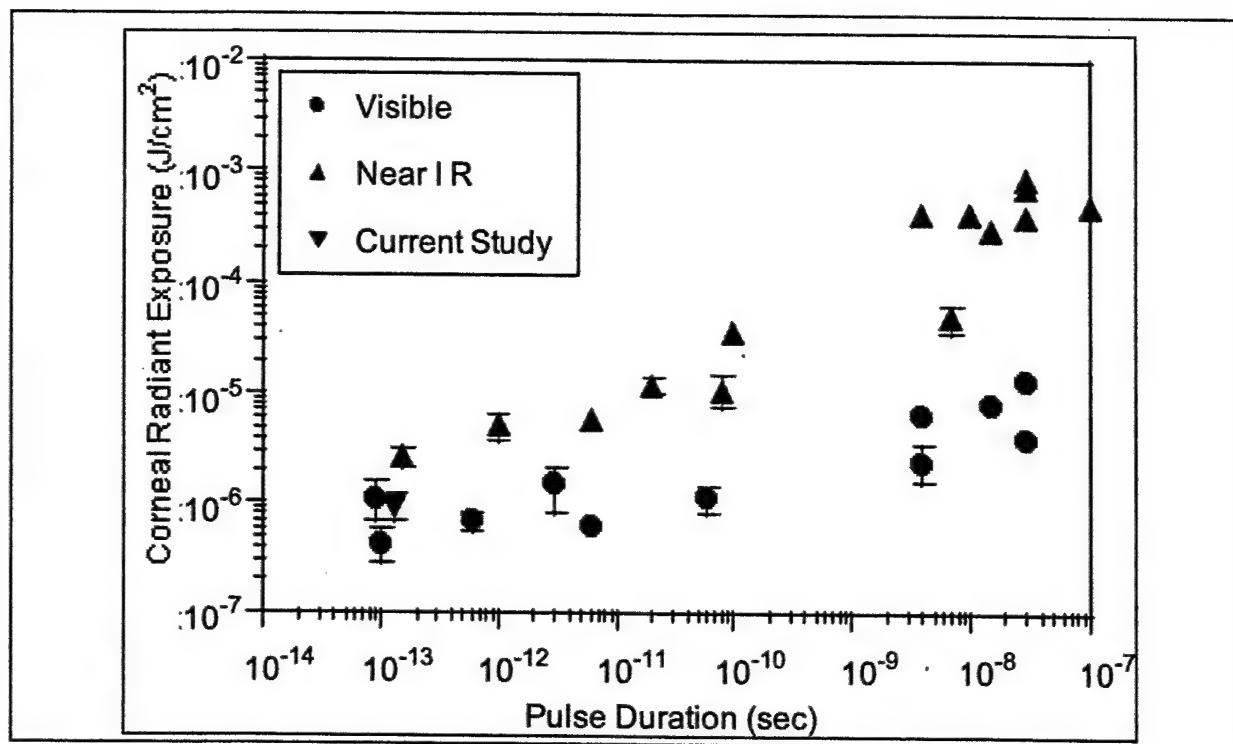
This study documents some of the shortest pulse width MVL exposures reported to date in the near-IR. Our macular  $ED_{50}$  value was 0.35  $\mu\text{J}$  at 130 fs. This represented the lowest threshold reported for all near-IR studies. [19], [18], [20], [7]. The value was slightly less than the 0.43  $\mu\text{J}$  recorded for the visible wavelength of 580 nm at 90 fs and one-third the value of 1.0  $\mu\text{J}$  measured at 1060 nm. However, this 0.35  $\mu\text{J}$  was double the 0.17  $\mu\text{J}$  measured at 530 nm for 100 fs. [7] Our data [7] indicate that as pulse duration decreases below 1 ns, the MVL thresholds at wavelengths in the visible and near-IR approach one another. Data at shorter pulse widths will

allow validation of observed trends. Figure 12 summarizes all MVL threshold data for single pulse exposures shorter than 10 ns.

Thresholds for the paramacular area were 1.6 times larger than the macular thresholds and this ratio held for both the one-hour and 24-hour data. Also, it is noteworthy that the  $ED_{50}$  threshold decreased by as much as 25 percent between the one-hour and 24-hour readings. We have observed similar trends in the past for other wavelengths (visible and near-IR) with pulses near 100 fs.

This study used the paramacular area that was 10 degrees temporal and 5 degrees inferior to the fovea. For comparison purposes and the limited availability of data that directly compares the sensitivity of the macula verses the paramacula, we compare our data to previous studies that reported values for the macula and the paramacula in the range of 30 degrees temporal to 30 nasal. These studies [52], [53], [54], [55] reported values that indicated the paramacula was less sensitive than the macula by a factor of 1.1 to 2 times. These studies employed different pulse widths and wavelengths from this study. Griess, et al. [55] reported on wavelengths on both sides of 800 nm for nanosecond pulses and found similar ratios for 1064 nm and 532 nm (1.47 at 1064 nm & 1.77 at 532 nm). The Griess study used a paramacular region immediately adjacent to the macula as in this study. Polhamus, *et al* [53] reported  $ED_{50}$  values for 532 nm at 10 ns pulse width for the macula and 30 degrees temporal. The ratios of these  $ED_{50}$ 's had a value of 2. Lappin, and Coogan [52] reported the lowest ratio (1.1) for a similar region of the retina for a five minute postexposure threshold. Thus this study's reported ratio of 1.6 is not significantly different from that of other reported pulse widths and wavelengths for similar regions of the fundus.

As in previous reports [12], [7] for ultrashort laser retinal exposures, fluorescein leakage from the smaller lesions could not be discriminated from the background choroidal flush. The FA thresholds for this pulse width were much higher than the MVL thresholds for both one-hour and 24-hour readings. In order to obtain statistically valid FA thresholds, significant additional higher-energy exposures would have been required. Because of the proven reduced sensitivity and the increased number of subjects that would have been required, FA thresholds are not reported here.



**Figure 12.** Minimum visible lesion thresholds for pulse widths shorter than 100 ns in the rhesus monkey (data from our laboratory are shown with error bars that represent the 95 percent confidence intervals).

### Data Set D: Multiple Pulse Thresholds

#### Experimental Overview

Retinal effects of multiple laser pulses were measured [56] almost thirty years ago and are still being measured today. [57] New pulse durations, wavelengths, pulse repetition rates and energies are now possible and their effects must be measured to extend the biological hazards database which supports establishment of safe exposure levels in laser safety standards.

Exposure limits to laser radiation are set by several national and international groups. These include the American National Standards Institute, [50] the International Commission on Non-Ionizing Radiation Protection [58], and the International Electrotechnical Commission [51]. These bodies currently differ in the evaluation of exposure limits for multiple femtosecond pulses. We have selected the recently published ANSI Z136.1-2000 exposure limits for a comparison to our data.

Maximum Permissible Exposures (MPE) and accessible emission limit (AEL) values have been set by the ANSI-Z136.1 Standard [50] for multiple pulse exposures. In the current ANSI standard, the method for calculating the MPE for multiple pulses has been procedurally improved [59]. There are three rules to follow in determining MPE values in the retinal hazard regime (i.e. 400-1400 nm), and the most conservative result of the three calculations is used in the hazard assessment for a given laser application. One rule calculates an MPE for a single pulse in a pulse grouping, and assures that no single pulse in the pulse-train is hazardous. This is seldom the most conservative MPE for pulses longer than one nanosecond, but is a significant restriction for sub-nanosecond pulses. A second rule protects against thermal or photochemical damage build-up and is calculated by taking the average power of any grouping of pulses in the pulse train. This rule protects against high-frequency lasers producing damage from small pulse energies when the average power surpasses the MPE for a CW pulse with an extended duration. The third rule is similar to what the previous version of the ANSI Z136 [60] used for a multiple-pulse correction factor, which reduces the single-pulse exposure according to the number of pulses ( $n$ ) raised to the negative one-quarter power ( $n^{-1/4}$ ). This correction factor was based on an empirical relationship found in experimental data which had shown that the ED<sub>50</sub> dosages for repetitive-pulse exposures expressed in terms of the total (of all pulses) intra-ocular energy were proportional to the pulse train duration ( $T$ ) raised to the  $3/4$  power for thermal injury.

This correction factor of ( $n^{-1/4}$ ) was first derived by Stuck, *et al* [61] for the reduction in pulse energy for multiple laser pulses for pulse duration down to 10 ns. A decrease in threshold ED<sub>50</sub> (J/cm<sup>2</sup>) has been shown by Griess [62] to be a function of the pulse duration " $t$ " raised to the  $3/4$  power for single pulse exposure durations ranging from about 18  $\mu$ s to 10 seconds. Griess *et al* [62] derived the relationship between the pulse repetition rate, pulse duration, and thermal relaxation time using a thermal model for the time-temperature profiles and the damage integral to predict a correction factor. They showed that the extremes for the correction factor for multiple pulses varied between unity when there was no additivity of damage such as very low repetition rates and the other extreme when the correction factor approaches  $1/n$ . Under this condition, the temperature rises linearly with each pulse because thermal relaxation is negligible due to a very high pulse repetition frequency (PRF). Thus, the correction factor should range from 1 to  $1/n$  depending on the PRF and the empirical ANSI correction factor ( $n^{-1/4}$ ) reflects the intermediate conditions of the experimental thresholds.

The first thorough study to be completed for the ocular effects of repetitive laser pulses was performed during the 1970s at the USAF School of Aerospace Medicine (USAF-SAM) for visible wavelengths and pulse repetition rates from single pulses to 10 kHz at a wavelength of 514 nm. [63] In parallel with this study at the USAF-SAM, two other studies were completed, [64], [65] for the ocular effects of near-infrared laser radiation using variable pulse durations and trains of microsecond and nanosecond pulses at 1060 nm. Following these three studies, two additional studies, [66], [67] were completed at the school which measured the ocular hazards of picosecond and repetitive pulses for visible and near-IR using variable pulse repetition rates and exposure times.

In all of these studies, the shortest pulse duration for visible wavelengths was in the microsecond range and for near-IR, it was in the nanosecond range. For a 270-ns single pulse at 1060 nm, the MVL threshold within the macula was 29  $\mu$ J and for the same laser at 1 kHz, the



threshold for 500 pulses was 1.98  $\mu\text{J}/\text{pulse}$ . For a visible wavelength of 514 nm, a single 10- $\mu\text{s}$  pulse had a threshold of 1.6  $\mu\text{J}$ . The threshold was 0.155  $\mu\text{J}/\text{pulse}$  for 500 pulses at a 1-kHz rate and the threshold then dropped to only 0.11  $\mu\text{J}/\text{pulse}$  for 5000 pulses at a rate of 10 kHz. [66]

Other researchers were taking similar measurements at or for USAF-SAM during that same time period with repetitive pulse lasers and found similar results. Gibbons & Egbert [68] measured thresholds for 40- $\mu\text{sec}$  pulses from an Argon laser and found the single pulse threshold to be 2  $\mu\text{J}$  while the threshold for 500 pulses at a rate of 1 kHz dropped to 1  $\mu\text{J}/\text{pulse}$ . Ebberts [69] measured the retinal damage thresholds using a gallium arsenide (GaAs) laser with a 905 nm wavelength for 30 ns pulses with a PRF of 1 kHz and constant power output from the laser. He increased the number of pulses (or on-time of the laser) until a lesion was produced. The study found that it took 0.7 seconds to produce a 50 percent probability of creating a visible lesion. Thus measuring the thresholds to be 0.32  $\mu\text{J}/\text{pulse}$  for 701 pulses.

Multi-pulse measurements at both 532 nm and 1064 nm (16-ns pulse duration) were taken for one and 100 pulses at a lower PRF of 10 Hz in both the macula and paramacula by Griess, *et al.* [55] For minimal retinal spot sizes ( $\sim 30 \mu\text{m}$ ) using a 10-second train of 532 nm pulses, the study found that the  $\text{ED}_{50}$  threshold in the paramacula dropped from 3.7  $\mu\text{J}$  for a single pulse to 0.52  $\mu\text{J}/\text{pulse}$  for 100 pulses or a drop in pulse energy of a factor of seven. In the macula, the threshold was reduced by a factor of almost 5 from 2.1  $\mu\text{J}$  to 0.44  $\mu\text{J}/\text{pulse}$ . For 1064-nm pulses, the threshold decreased in the paramacula by a factor of 2.8 when going from a single pulse to 100 pulses in a 10 sec train (45  $\mu\text{J}$  to 16  $\mu\text{J}/\text{pulse}$ ). Similarly, the study found that the  $\text{ED}_{50}$  macula threshold decreased by a factor of 2.7 (30  $\mu\text{J}$  to 11.3  $\mu\text{J}/\text{pulse}$ ) for the same increase from 1 to 100 pulses. Their ratios for the paramacula/macula  $\text{ED}_{50}$ 's at 24 hours were 1.8 for the 532-nm visible pulse and 1.5 for the 1064-nm near-IR pulse.

Thresholds for retinal effects from single laser ultrashort pulses have been reported [12] for pulsewidths as short as 90 femtoseconds and wavelengths from 530 nm to 1064 nm. Other short, multiple pulse thresholds have been reported [65], [66], [67], [68], [69], [55] for various wavelengths, pulse durations and number of pulses. However none were in the femtosecond pulse regime. Most of the previously reported thresholds for multipulse have been for 514 nm, 530 nm or 1060 nm and pulse duration from 6-ps and longer.

### Minimal Visible Lesion Thresholds

The laser system described as Laser System II was used for this multiple-pulse study. The system is illustrated in Figure 2. Marker lesions were produced with a krypton gas laser operating at 647 nm. The krypton laser was shuttered to a yield 3- to 4-ms pulse and the output power was adjusted to give a consistent high-contrast, white marker lesion.

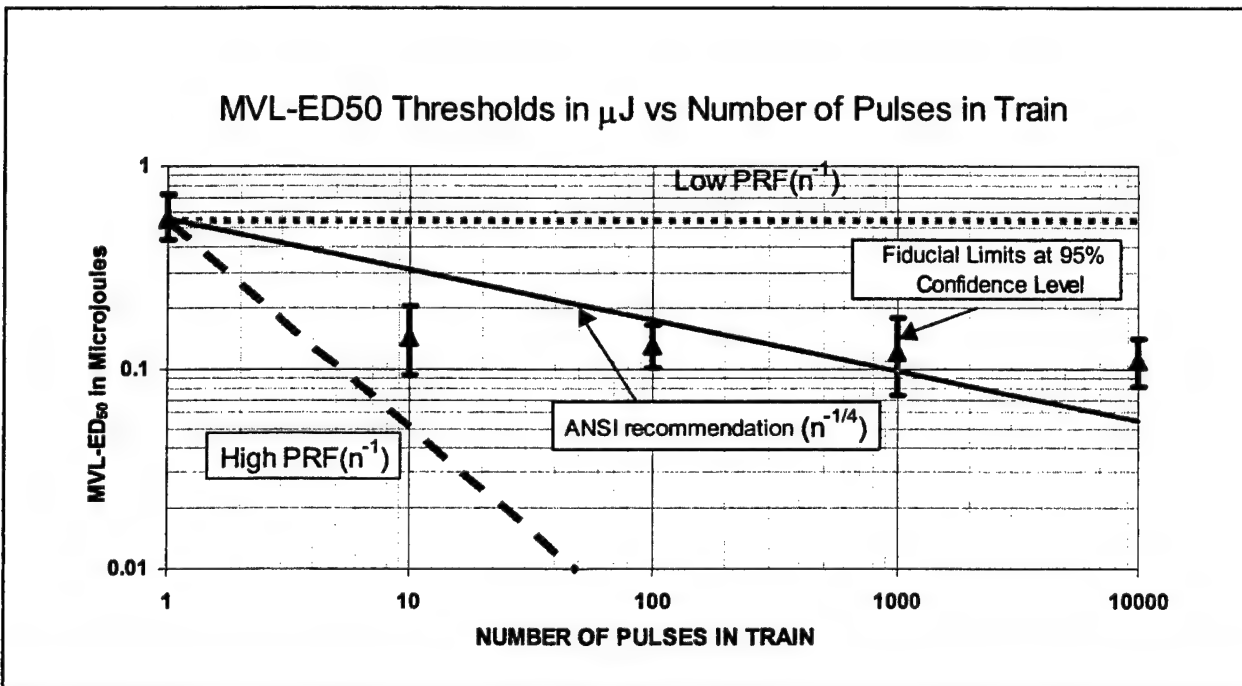
All data for the multiple-pulse thresholds taken in the paramacula are listed in Table 7 for both the one-hour and 24-hour post exposure. Fiducial limits at their 95 percent confidence level are in parentheses next to the thresholds and in the last column are the slopes of the probit curves for the 24-hour readings. The threshold in the paramacula for single pulses at



24-hours post exposure was 0.55  $\mu\text{J}$  while the threshold for 10 pulses dropped to 0.15  $\mu\text{J}/\text{pulse}$ . Increasing the number to 10,000 pulses did not decrease the thresholds significantly.

Number of Pulses	1-hr Reading MVL-ED <sub>50</sub> ( $\mu\text{J}/\text{pulse}$ )	24-hr Reading MVL- ED <sub>50</sub> ( $\mu\text{J}/\text{pulse}$ )	Slope of Probit Curve (24-hr Data)
1	0.65 (0.51 – 0.91)	0.55 (0.44 - 0.73)	2.5
10	0.38 (0.22 – 1.05)	0.15 (0.09 – 0.21)	2.8
100	0.24 (0.17 – 0.37)	0.13 (0.10 – 0.17)	4.1
1,000	0.66 (0.28 – 14.6)	0.12 (0.07 – 0.18)	1.7
10,000	0.23 (0.16 – 0.38)	0.11 (0.08 – 0.14)	4.7

**Table 7.** Visible lesion thresholds for multipulse laser shots at one and 24hours post exposure (paramacular). Fiducial limits listed in parenthesis, slopes at 24-hours post exposure.



**Figure 13.** Multiple pulse MVL thresholds as a function of number of pulses in the train. Energy is shown as microjoules per pulse.

The thresholds listed in Table 7 have been plotted in Figure 13 together with their fiducial limits as error bars for the single pulse paramacula data point together with the four decades of pulses. A solid, straight line was drawn through the four multiple-pulse data points only as an aid in viewing the data.

Also plotted in this figure are the curves for  $Q(1)$ ,  $Q(n^{-1/4})$  and  $Q(n^{-1})$  using the number of pulses times the single-pulse threshold value ( $Q = 0.55 \mu\text{J}$ ). These broken line curves show how the thresholds would decrease for repetitive pulses if they followed the ANSI-Z136.1 Standard for ( $n^{-1/4}$ ) or when all pulses were additive and the thresholds were reduced by ( $1/n$ ). The ANSI standard has a constant decrement of 1.78 per decade for the total number of pulses as shown in the figure whereas the ( $n^{-1}$ ) dashed straight line has a constant decrement of 10 per decade.

### Fluorescein Angiography Thresholds

All fluorescein angiographic data (FAVL-ED<sub>50</sub>) are listed in Table 8 for both one and 24-hour readings as for the fundusoscopic thresholds. It was not always possible to obtain the fiducial limits for the FAVL and there was wide variability in the thresholds calculated by the probit analysis. As shown in Table 8, the thresholds at the 24-hour reading were not always lower than the 1-hour thresholds as they were for the MVL thresholds. For all of the multipulse data, the highest threshold measured was 3.5 mJ at the 24-hour reading for 1,000 pulses and the lowest FAVL-ED<sub>50</sub> was 0.43  $\mu\text{J}$  measured for 10,000 pulses at the one-hour reading. All other thresholds ranged between these two extremes.

Number of Pulses	1-hr Reading FAVL-ED <sub>50</sub> ( $\mu\text{J}/\text{pulse}$ )	24-hr Reading FAVL-ED <sub>50</sub> ( $\mu\text{J}/\text{pulse}$ )
1	2.56 (1.78 – 8.6)	1.65 (0.93 – 2.88)
10	2.63 (0.55 – XX)	1.50 (0.59 – XX)
100	0.92 (0.62 – 2.1)	0.92 (0.62 – 1.92)
1,000	1.97 (0.59 – XX)	3.51 (0.78 – XX)
10,000	0.43 (0.25 – 2.31)	0.65 (0.40 – 121)

**Table 8.** Fluorescein angiographic visible lesion thresholds for multi-pulse laser shots at one and 24-hours post exposure. Fiducial limits at their 95 percent confidence level in parenthesis.

## Discussion

The data reported in this study are the only known multiple-pulse, sub-picosecond data available at 800 nm. Even though exposures were placed in the paramacula, they can be compared it to previous single-pulse data at 130 fs as well as other multiple-pulse studies by considering relative sensitivity of the macula and paramacula to laser damage. In a previous study, Cain *et al.* [9] measured the relative sensitivities of the macula and paramacula to these ultrashort laser pulses, and reported a paramacula-to-macula ratio of 1.6. These results can also be compared to other data reported in the literature at different wavelengths, pulse durations and pulse repetition rates in the macula and paramacula.

Our MVL-ED<sub>50</sub> threshold for the single pulse (Table 7) of 0.55  $\mu\text{J}$  at 24-hours post exposure for this 800 nm data does fall between the 0.16  $\mu\text{J}$  at 530 nm and the 1.0  $\mu\text{J}$  at 1060 nm at 130 fs measured in our laboratory.[7] We have also reported the MVL-ED<sub>50</sub> threshold of 0.43  $\mu\text{J}$  for the 580 nm wavelength, taken at 90 fs within the macula. [12] This slight difference (0.43 vs 0.55  $\mu\text{J}$ ) between thresholds for the 580 nm and 800 nm wavelengths could somehow be related to the maximal absorption of blood at the 577 nm wavelength and very little absorption at 800 nm.

Our FAVL thresholds for fluorescein angiography were higher than the MVL thresholds by a factor of six or more and these higher thresholds are consistent with all of our previous measurements for both visible and near-IR thresholds within the primate eye. In our previous measurements at 580 nm and 90 fs, the ophthalmoscopic readings for lesions were seven times more sensitive than fluorescein angiography. Also, for the 1060 nm at 150 fs, ophthalmoscopic readings for lesions was 12 times more sensitive than fluorescein angiography.[12] [7] However, it should be noted that our fluorescein angiographic techniques did show a higher sensitivity at these femtosecond pulses in the rabbit eye.[24] Due to the lower sensitivity of FA, this data will not be discussed further.

The multiple pulse thresholds decreased between one and 24 hours by a factor of two or more for each number of pulses from 10 to 10,000. Connolly *et al* [66] found this same drop of a factor of 2 for 514 nm with 10  $\mu\text{s}$  pulses for all measurements of 30 pulses and higher. Griess, *et al* [55] reported a 20 percent drop between the one and 24-hour readings for single pulses at 1064 nm and 16 ns pulsewidth and a 40 percent drop after 24 hours for repetitive pulses from 10 to 100 in the paramacula. For their 532 nm pulses, the drop in threshold for single pulses were only 6 percent while for 100 pulses, it had a drop of 45 percent or almost by a factor of 2. It appears the drop in threshold at 24 hours is more significant for shorter pulse durations (ultrashort, Q-switched) than for longer exposures (microsecond and longer).

The uppermost dotted line in Figure 13 represents the damage threshold trend expected from a pulse train where the single-pulse threshold was the most conservative case, and there is no additivity attributed to earlier pulses. The dashed line shown in Figure 13 represents the decrease in threshold if it followed a factor of  $(n^{-1})$ , which was first derived by Griess and Blankenstein [62]. This factor represents the case where there is total additivity of the effects of laser exposures within the retina and the threshold per pulse decreases proportionally to the

number of pulses. The solid line in Figure 13 represents the intermediate  $n^{-1/4}$  multiple-pulse correction factor used in the ANSI laser safety standard for thermal damage mechanism additivity.

The data from this study show that any cumulative effect on damage thresholds for multiple femtosecond laser pulses occurs only for the first few pulses and does not follow either the  $(n^{-1/4})$  or  $(n^{-1})$  curves shown in Figure 13. Also, the data seem to approach a minimum pulse energy below which these laser pulses do not produce an observable lesion regardless of how many pulse there are in a train. In an attempt to explain this sudden drop in thresholds between 1 and 10 pulses, the pulse-to-pulse energy variations of the pulse trains were measured. Every pulse train applied to the eye was measured and recorded for its mean pulse energy, standard deviation, minimum and maximum energies, and the ratio of maximum to minimum. This data was carefully analyzed for the trains of 10 pulses and it was found that the max/min ratios varied only 5 percent on the average with a peak of only 10 percent above the average energy. Therefore, the pulse-to-pulse variations could not account for the 70-percent drop in threshold.

Others, using multiple-pulse trains for up to 30 seconds for both visible and near-IR, have also reported this reduction in threshold for the first few pulses in biological systems. Connelly *et al.* [66] measured the thresholds for variable PRFs from single pulses to 10 kHz for a 5-second train of 10- $\mu$ s, 514-nm pulses. Their single-pulse threshold was 1.61  $\mu$ J and for 5 pulses, dropped to 0.25  $\mu$ J/pulse and remained at that level up to 5,000 pulses. They stated, that for a 5-second train with varying number of PRFs and number of pulses "within experimental error, there is no difference between the thresholds for 50 and 300 pulses at 10 Hz and that the damage observed after 300 pulses was induced by the first 50." Also for 1-Hz PRF and pulse trains of 5 and 30 pulses, there was no difference between thresholds for 5 pulses and 30 pulses. Thus the first 5 pulses induced the damage observed with 30 pulses. Hemstreet *et al.* [67] found similar results with the near-IR wavelengths and varying pulse trains.

There has been one set of in-vivo data reported with comparable repetition rates, which can be reasonably compared to this study. The most comparable data reported [69] was for a 905-nm, 30-ns pulse duration, GaAs laser operating at 1 kHz and had an output of 0.32  $\mu$ J/pulse with a peak pulse power of 5.5 kW. The researcher was not able obtain a single-pulse threshold with this repetition rate but was able to measure the threshold in a primate eye by varying the length of the pulse train and the number of pulses. The threshold at one hour was found to be 0.7 seconds or 701 pulses at 0.32  $\mu$ J/pulse. The nearest comparable data point in the current study was for 800 nm at 130-fs pulse duration with 1,000 pulses in one second, one-kHz PRF, giving an ED<sub>50</sub> of 0.12  $\mu$ J/pulse. Considering the differences between nanosecond and femtosecond pulsed lasers, this difference in damage threshold is much less than would be expected for single pulses at the same pulse widths (30 ns vs 130 fs).

An ex-vivo study recently reported thresholds for porcine multiple pulse exposures [70]. Lasers that produced pulses of 527 nm, between 250 ns and 3 ms at a PRF of 500 Hz were used in the study. Thresholds for cellular damage were evaluated using a fluorescence viability assay. Similar trends were shown where significant threshold reduction occurred between one and ten pulses, and little additional variation up to 10,000 pulses. An exhaustive application of thermal models provided an inconclusive inference of the damage mechanism. Although the

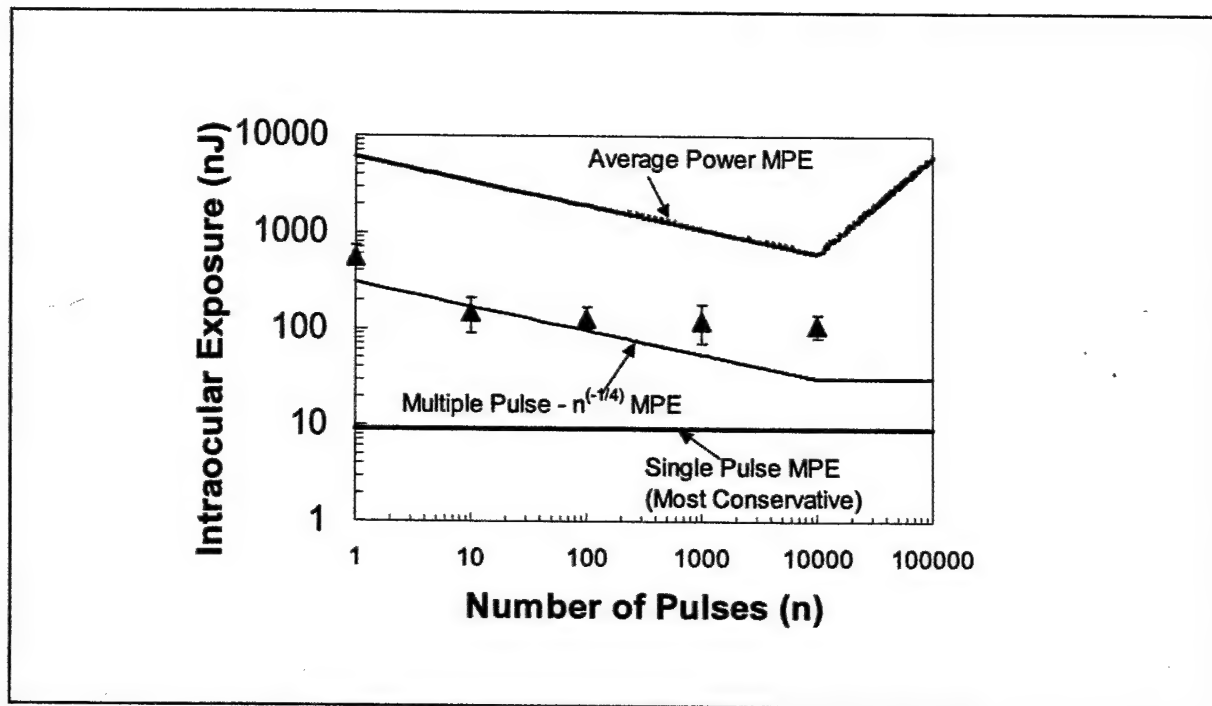
complexity of the system does not currently allow mathematical models to provide accurate trends, the experimental data is similar to our experimental in-vivo trends.

When considering sub-picosecond laser pulses, the possibility of laser-induced breakdown (LIB) as a primary or secondary mechanism for damage must be taken into account. These ultrashort pulses can produce extremely high peak powers. Recent studies [38] have made comparisons of biological damage studies to non-biological systems as well as to theoretical work. These comparisons have determined that for pulses near 100-fs in duration, predicted LIB thresholds are very near the experimentally established damage thresholds. With this information in mind, we have examined very recent theoretical and non-biological experimental work that has been presented determining damage thresholds from multiple-pulse, 1-kHz exposures from sub-picosecond lasers. [71, 72] The experimental studies have shown very similar trends in damage thresholds when compared with our data, indicating a modest decrease in damage threshold over the first few to tens of pulses applied. Theoretical models do not predict these trends, leading the researchers to speculate that there is some small damage event occurring that is below detection threshold, and is then emphasized by the following pulses.

These new data were also compared to the new exposure limits prescribed by the new ANSI Z136.1-2000 Standard [50]. Recent updates to the ANSI Z136.1 Standard [1, 73] have incorporated a great deal of new biological data, including ultrashort pulse durations. It is critical that new data can be consistently compared to established safety thresholds.

The ANSI Standard "Three Rule Method" was applied to each experimental point and the MPE was computed for each of the three rules. The resulting MPEs (multiplied by the area of the appropriate limiting aperture for comparison in Joules) are plotted along with the experimental data in Figure 14. The three rules are each identified by their respective trends, with the single-pulse MPE being the most conservative for the experimental conditions. In a hazard assessment this single-pulse MPE would be applied. Our data indicates that the ANSI Standard provides a consistent safety margin of at least one order of magnitude for all pulse numbers, even though it does not reflect the early reduction in damage threshold between one and ten pulses.

There are several conclusions that may be drawn from our data regarding visible lesion thresholds due to multiple-pulse lasers. Again, we have shown that the fluorescein angiographic technique for determining lesion thresholds is not as sensitive in measuring thresholds as the direct ophthalmoscopic observation. This data confirmed all of our previous measurements within the primate eye.



**Figure 14:** Comparison of 800-nm, 1-kHz PRF, 130 fs minimal visible lesion data (triangles) to the three MPE values (expressed in joules by multiplying the area of the appropriate limiting aperture) computed from the ANSI Z136.1-2000 Standard. The data indicate that the damage threshold is consistently one order of magnitude higher than the prescribed MPE from the ANSI Standard selected as the "Single Pulse MPE" as labeled in the graph.

It seems reasonable to conclude that the visible lesion thresholds for these 130 fs pulses at 800 nm, do not follow any single established trend. During the first 10 pulses of a repetitive pulse laser with a PRF of 1 kHz, the MVL threshold drops much faster than the multiple-pulse ( $n^{-1/4}$ ) correction factor predicts (a ratio of 3.7 actual versus 1.8 predicted). The threshold remains nearly constant thereafter with only a 10 percent decrement for each decade increase in the number of pulses. It was found that a minimum pulse energy of 110 nJ/pulse was needed for damage using pulse trains (130 fs, 800 nm, 1 kHz) from 10 ms out to 10 seconds. Thus it may be concluded for multiple-pulse exposures greater than 10 pulses, that there is no significant decrease in retinal damage threshold observed within the fundus of the eye for a sub-picosecond, 1-kHz pulse train.

The MPE values obtained through the application of the "Three Rule Method" found in the ANSI Z136.1-2000 Standard provide an adequate measure of safety for ultrashort, 1-kHz pulse train, near-infrared lasers over a broad range of exposure durations. Damage mechanisms responsible for the decrease in thresholds for the first few pulses are not well understood, and are not predicted by current theoretical models. They warrant further investigation through experimental and theoretical work.



## **Data Set E: Mode-Locked and CW Thresholds**

### **Experimental Overview**

Current laser technology has demonstrated that sub-picosecond and even sub-100 femtosecond mode-locked laser systems can be produced affordably and can be constructed to require minimal operator maintenance. [74] These qualities have proven to be of enormous benefit in medical treatment settings with Q-switched and continuous-wave (CW) output lasers. Several technical benefits are associated with the use of mode-locked lasers in clinical applications. The high peak-power (individual pulse energy divided by the pulse duration) contained in individual pulses provides an efficient method of frequency-doubling the laser, producing a green beam from an infrared one, for example. These high peak-powers can also be used for a new type of three-dimensional imaging technique, two-photon absorption, which creates a confocal microscopy-type image. The laser beam can be scanned to produce a three dimensional reconstruction [75] or can be used for two-photon activation in photodynamic therapies. Mode-locked lasers with extremely short pulse duration ( $< 50$  fs) have been used to improve optical coherence tomography (OCT) images. Femtosecond lasers have also been used recently in ophthalmic applications, demonstrating photodisruption with reduced collateral damage compared to nanosecond pulses. [76] These exciting developments provide part of the impetus for our studies.

There are other advantages to using a mode-locked laser over the conventional CW laser. Ultrashort pulse mode-locked lasers can often be tuned over a broad wavelength range. The typical Titanium: Sapphire laser can be used over the range of about 780 to 1000 nm in the near infrared, and can be frequency-doubled or -tripled to access wavelengths in the visible and ultraviolet. Using frequency-mixing techniques, these mode-locked lasers can also produce multiple wavelengths simultaneously from a single laser source.

The determination of ocular damage thresholds for ultrashort laser pulses is also of current interest in the establishment of laser safety exposure limits.[1, 77] In particular, the standards must address the exposures to pulse trains from sub-picosecond, mode-locked lasers. These lasers commonly operate with a pulse repetition frequency (PRF) of approximately 50 to 100 MHz. Minimal visible lesion (MVL) thresholds have been determined for several categories of pulsed laser exposures and are strongly dependent upon the PRF of the system and the duration of the exposure. Current laser standards define a maximum PRF at which thermal damage thresholds for repetitively pulsed lasers become indistinguishable from those for CW systems. This has not been tested for ultrashort exposures, but is extremely important for devices, which incorporate ultrafast lasers such as LIDAR and virtual retinal display systems.

Our laboratory has conducted several studies, to determine ultrashort laser pulse retinal MVL thresholds in the visible and near-infrared regions of the spectrum. These studies have determined single pulse thresholds for pulse durations of approximately  $10^{-8}$  to  $10^{-13}$  seconds. Although these studies have primarily focused on single-pulse thresholds, recent work [78] to establish multiple-pulse damage threshold trends has been completed at a PRF of 1 kHz. This



study determined that for pulses of 130-femtosecond duration, the damage thresholds do not follow common trends as a function of the number of pulses (i.e.  $n^{-1/4}$ ). New damage mechanisms come into play in the ultrashort regime; complicating the traditional understanding from thermal models. This is a significant implication for the establishment of laser safety standards. For the purposes of this study, we will primarily refer to the American National Standards Institute (ANSI) American National Standard for Safe Use of Lasers, Z136.1-2000. This is a consensus user standard currently employed in the United States [50]. Similar exposure limits have been adopted by the international laser safety standard, the IEC 80625-1 published in 2001 [51]. The United States Federal standard, Code of Federal Regulations 1040.10 and 1040.11, is currently considering harmonization and adoption of the sub-nanosecond exposure limits.

At high PRF, the damage threshold is anticipated to approach the CW laser threshold. This has been observed with longer pulse-duration trains [55]. At high PRFs, thermal models can accurately predict tissue damage mechanisms. In order to anchor thresholds to previous measurements and extend the mode-locked exposure findings to include femtosecond pulses, a direct comparison with CW lasers is necessary.

Here we have designed a direct comparison of CW and mode-locked exposures with identical beam diameters, beam divergence and wavelength. Note that the creation of ultrashort pulses requires increased bandwidth (a larger wavelength spread) when compared with the CW exposure. However we have centered both exposure conditions at the same center wavelength. We believe that this is one of the most direct comparisons to date in an MVL threshold experiment.

#### Minimal Visible Lesion Thresholds

The results for one-quarter second exposure to CW and mode-locked pulse trains at 76 MHz are summarized in Table 9. A probit data analysis technique was applied to the "yes/no" recorded as a one or zero for each dosage applied. The Estimated Dosage to cause a MVL with 50-percent probability is given in each case. Values are reported at 24-hours post exposure. Fiducial limits for the  $ED_{50}$  numbers are also provided. These represent intervals at 95 percent confidence. The final column indicates the slope of the probit curve measured at the  $ED_{50}$  value point. In each case, the slope is greater than 2.0 for the 24-hour data, which is characteristic of good data. This was one of the criteria for ending the experiment. The second criterion was that the fiducial limits as computed at the 95-percent confidence interval were within a factor of 0.5 to 1.5 of the  $ED_{50}$  value. As is illustrated by the data, both criteria are met for the 24-hour post exposure data.

Laser Mode	Exposure Duration (s)	Wavelength (nm)	24-hr Reading MVL-ED <sub>50</sub>	Fiducial Limits	Slope of Probit Curve (24-hr Data)
Mode-Locked 130 fs, 76 MHz	0.25	800	5.90 mJ 23.6 mW	5.23 – 6.60 mJ 20.9 – 26.4 mW	7.85
CW	0.25	800	5.84 mJ 23.4 mW	5.23 – 6.58 mJ 20.9 – 26.3 mW	8.01

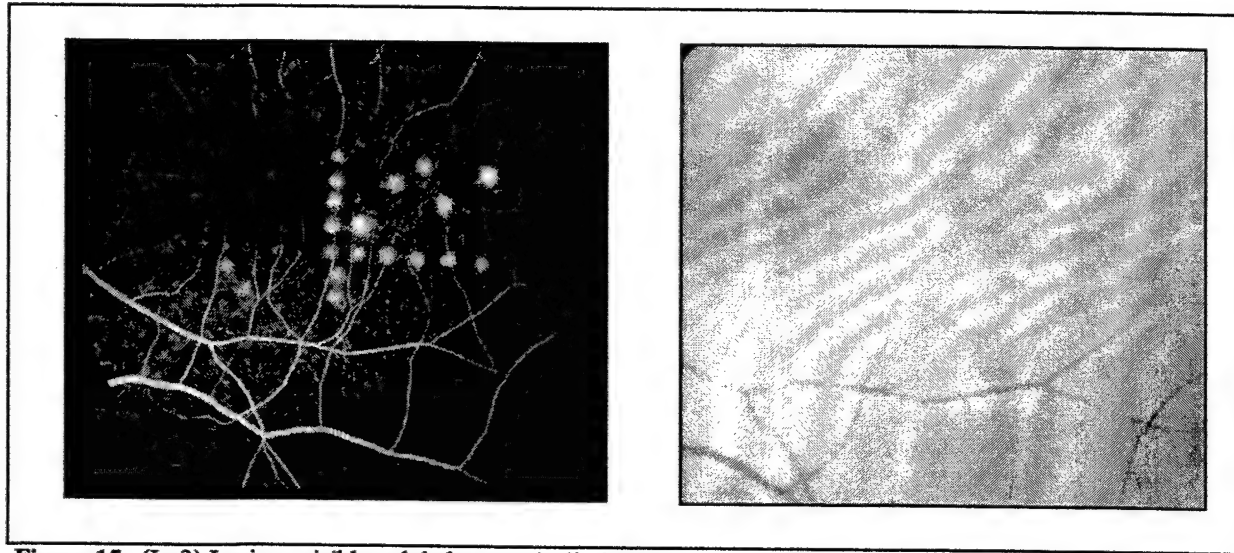
**Table 9.** Mode-Locked vs. CW MVL Threshold Experimental Results – Ophthalmoscopic.

Laser Mode	Exposure Duration (s)	Wavelength (nm)	24-hr Reading FAVL-ED <sub>50</sub>	Fiducial Limits	Slope of Probit Curve (24-hr Data)
Mode-Locked 130 fs, 76 MHz	0.25	800	6.71 mJ 26.8 mW	6.12 – 7.47 mJ 24.5 – 29.9 mW	10.3
CW	0.25	800	6.04 mJ 24.2 mW	5.41 – 6.89 mJ 21.6 – 27.6 mW	7.68

**Table 10.** Mode-Locked vs. CW MVL Threshold Experimental Results – Fluorescein Angiography.

### Fluorescein Angiography Thresholds

Fluorescein angiographic threshold data are listed in Table 10, for 24-hour post exposures along with the slopes of the probit curves for the 24-hour readings. For both CW and mode-locked laser exposures, the threshold for FA visibility was higher than the threshold for MVL. The threshold for FAVL at 24 hours was observed to be approximately 15 percent higher than Ophthalmoscopically visible MVL thresholds. However, the slopes of the probit curve for the mode-locked data improve slightly for FAVL. Side-by-side comparison of FAs and fundus photographs demonstrate a few sites of visible retinal laser lesions without FA evidence of damage. It is important to note, however, that the threshold values agree to within the fiducial limits for 95 percent confidence limits in the probit analysis.



**Figure 15.** (Left) Lesions visible ophthalmoscopically in FAVL photograph. (Right) . Lesions visible ophthalmoscopically in fundus photograph.

### Discussion

We report a final value for our study of 6.14 mJ (4.97 – 7.27 mJ) and 5.77 mJ (5.04 – 6.50 mJ) for mode-locked and CW paramacular exposures, respectively, at 24-hours post exposure. The equivalent CW exposure average powers are equivalent to 24.6 and 23.1 mW for the same thresholds. We find that these values represent equivalent MVL thresholds for the two exposure conditions at  $\frac{1}{4}$ -seconds exposure. The difference is less than 0.4 mJ and the confidence intervals overlap significantly.

The MVL thresholds presented here represent an excellent agreement with previous CW and mode-locked laser studies. In order to make the best comparison with published data, we have examined studies with exposure times near the  $\frac{1}{4}$ -second value of our study. Table 11 lists several MVL values, which were selected for comparison. The studies were selected based upon exposure duration, wavelength, and subject.

To our knowledge, there is no data at one-quarter second, 800 nm in the open literature. Several studies exist at nearby wavelengths, particularly 632 nm (HeNe), 647 nm (Kr+), 1060 (Nd:Glass), and 1064 nm (Nd:YAG). The studies of Lund et al [79], [80], [81], [82] map one-tenth second CW exposure thresholds for Ti:Sapphire lasers in the range of 700 to 1000 nm. Several values extracted from the literature have been assembled for Table 11. The comparable data largely consists of CW exposures of 0.1 to 1 second in duration. In each case, we have normalized the data to a  $\frac{1}{4}$ -second exposure duration by applying the ANSI Z136.1-2000 Standard's trend of MPE's following time to the three-quarter's power. Figure 16 illustrates the data obtained from the literature. This normalization brought the various studies into good agreement, with variations of up to about a factor of two at a given wavelength. Other variations can be attributed to lesion placement in macular or paramacular regions of the retina, observation

times, while some variations in the data can be attributed to variation in retinal spot size due to the wavelength, beam diameter and divergence characteristics of the particular laser used.

We could find no data for mode-locked, sub-picosecond exposures for rhesus subjects. Studies for longer pulse widths can be examined, however. The most directly comparable is the data available for 1064 nm. The references from Lund [83], Connolly [66], Skeen *et.al.*[64] and Birngruber *et.al.* [84] These references contain values for 1064 nm and 1060 nm exposures, both mode-locked (300 ps, 200 MHz) and CW. Figure 16 shows that at that wavelength the different studies compare well. There, the mode-locked point is normalized from a one second exposure, the largest difference extrapolated.

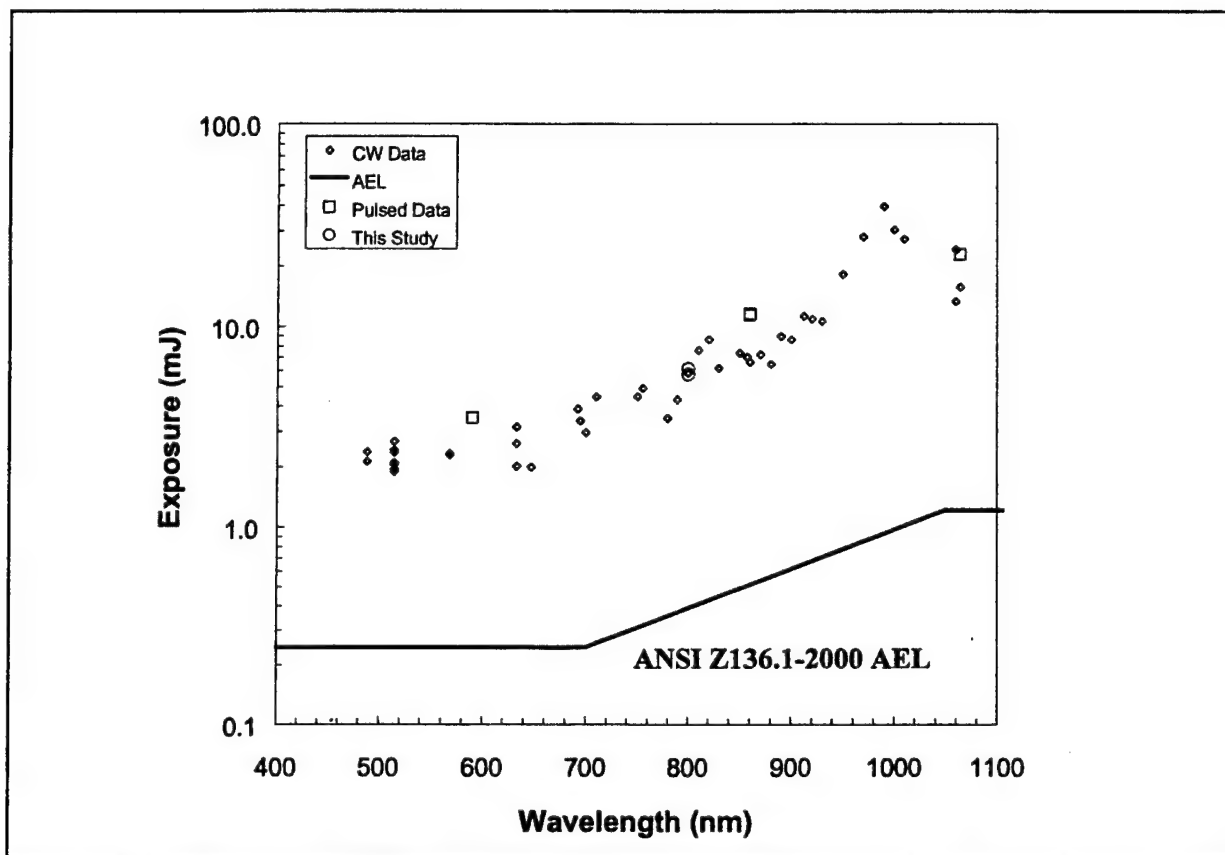


Figure 16. MVL thresholds for visible and near-IR wavelengths, normalized to one-quarter second exposure duration. Circular points represent repetitively pulsed thresholds in the quasi-CW limit. Diamonds indicate true CW exposures and circles represent our current study.

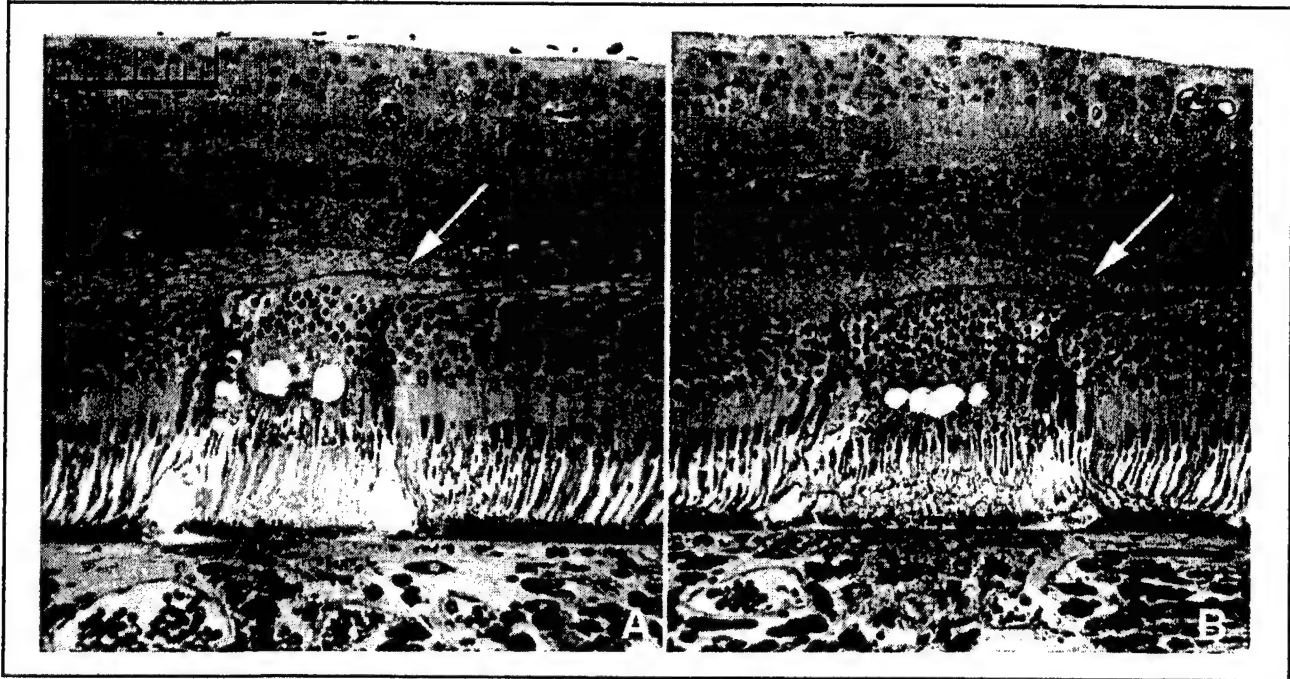
Also available are the studies by Courant *et al* [57] who performed an MVL study using 8-ps, 590-nm, laser pulses in a 0.2-second, 1-MHz PRF pulse train. That study did not make a direct comparison with CW exposures. Another study documented by Lund, *et al* [85] using a GaAs diode laser (860nm) repetitively pulsed at 120 kHz PRF, with 500-ns pulses also determined an MVL threshold for 0.125-second and 0.5-second exposures. These two studies are represented by the squares in Figure 16. Again, no direct comparison was made with CW exposures.

From Table 11 and Figure 16, we see that our study follows closely the CW trends as a function of wavelength at  $\frac{1}{4}$ -second exposure duration. The two adjacent wavelengths, 647 nm and 860 nm, have lower and higher MVL thresholds when normalized to 0.25-second exposure times. This is expected, following the prescribed wavelength dependence in MPE from the ANSI Z136.1-2000 Standard.

Our data indicate that average power dictates the damage threshold for the 800-nm, 76-MHz mode-locked, 100-fs laser. This experiment has provided the most direct comparison of damage thresholds possible, with nearly identical beam propagation parameters for both laser exposures. These results point to a thermal damage mechanism as has been described in prior work with CW lasers.

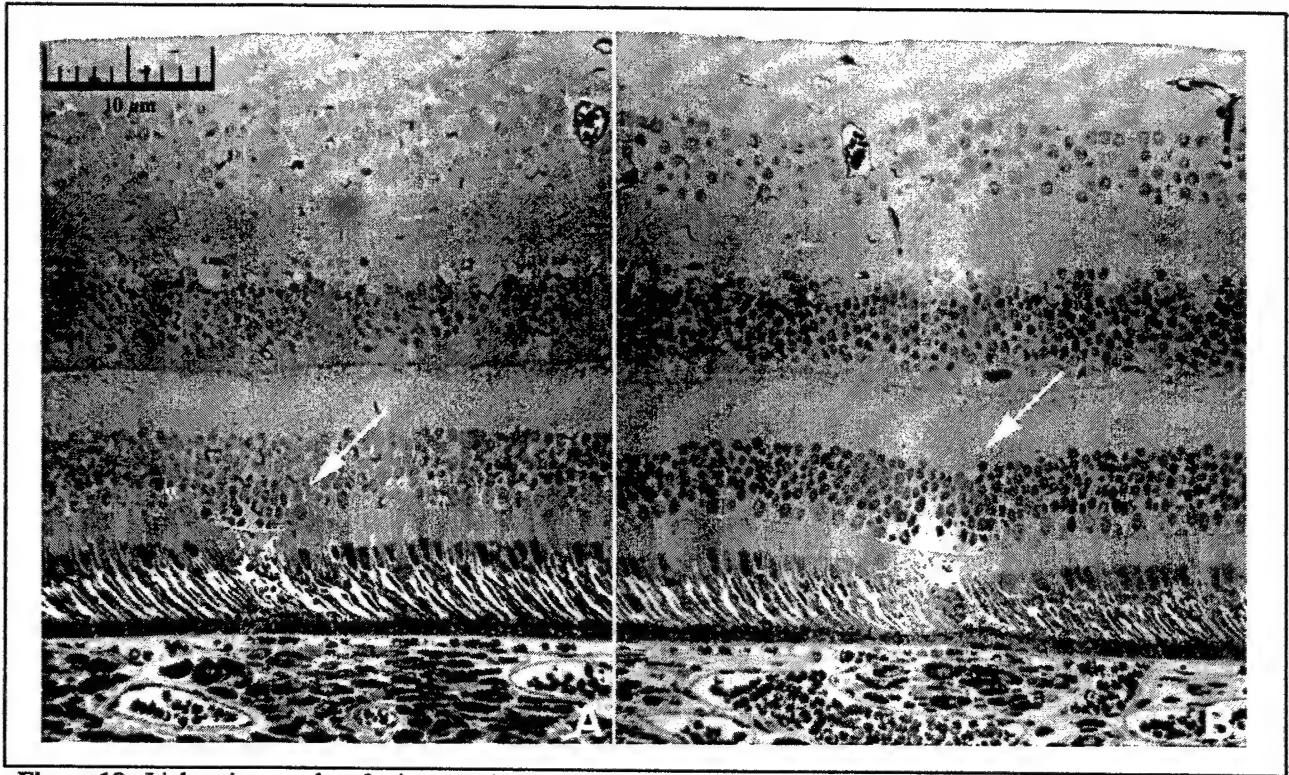
A total of 36 sites of acute laser-induced retinal lesions, 21 CW and 15 mode-locked, and 33 sites of 2-month-old, laser-induced retinal lesions, 18 CW and 15 mode-locked were examined with white-light microscopy of fixed sections. In both the CW and the mode-locked groups, there was one lesion site in each group in which no damage was found. This may be due to limitations in processing and sectioning the tissue.

Acute lesions had similar gross morphology in both the mode-locked and CW lesions within the same parameters (Figure 17 and Figure 18). Cross-sections of acute (< 1hr old), high-energy, 12.5-mJ (50 mW for 0.25 s) mode-locked and CW pulse sites revealed domed lesions with abnormal nuclei, photoreceptor damage, retinal pigment epithelium (RPE) damage and extensive choroidal damage (Figure 17A & B). Bruch's membrane was affected in all lesions, but had no sites of rupture in either group of lesions. Both CW and mode-locked lesions had damage that spread hundreds of microns transversely through the outer plexiform layer (arrowheads in Figure 17 A & B) in a pattern similar to that previously reported from CW-argon, 70-mW lesions [86].



**Figure 17.** Light micrographs of primate retina, stained with toluidine blue, showing acute (< one-hour old) laser lesions. **A.** Lesion produced by 50mW continuous wave laser beam of 800-nm wavelength for a 0.25-s duration delivered to the cornea, energy 12.5 mJ; **B.** Lesion produced by 50-mW mode-locked laser beam with 130-fs pulses at 76 MHz for 0.25 s, actual energy 12.5 mJ. Note the focal zone of laser injury to the outer retina and choroid (white arrows) with pyknotic photoreceptor nuclei, disruption of photoreceptor outer segments, vacuolization of the RPE and thrombosis within the choriocapillaris. There are large vacuoles near the outer margin of the RPE damage and centrally in the region of the photoreceptor inner segments. There is a darkening of the photoreceptor axons extending laterally through the outer plexiform layer (black arrows).





**Figure 18.** Light micrographs of primate retina, stained with toluidine blue, showing chronic (2 month old) laser lesions. **A.** Lesion produced by a 30-mW continuous wave laser beam of 800-nm wavelength for 0.25 s, actual energy 7.5 mJ; **B.** Lesion produced by 30-mW mode-locked laser beam with 130-fs pulses at 76 MHz for 0.25 s, actual energy 7.5 mJ. Note the focal zone of persisting laser injury to the outer retina and choroid (arrows). At this time point, few abnormal photoreceptor nuclei remain, there is a curved depression in the external limiting membrane and the RPE is stacked over the base of the lesion.



The acute 40-to-50 mW lesions displayed a statistically significant difference ( $p < 0.001$ , Fisher's Exact Test) between the CW and mode-locked groups in appearance of the damaged outer photoreceptor nuclei. The CW group had 18 of 21 (86 percent) category B nuclear damage, with two lesions category D and one category C. In contrast, the mode-locked lesions had 9 of 15 (60 percent) category A nuclear damage and 5 of 15 (33 percent) category B, with one lesion site category C. Thus the mode-locked lesions were more frequently of a pattern of evenly dispersed pyknotic photoreceptor nuclei when compared to the uneven pattern of damage in the nuclei of the CW lesions (Figure 17 A & B).

The acute 40 to 50 mW lesions also displayed a statistically significant difference in horizontal lesion size. The horizontal diameter of the lesion for both the RPE and the photoreceptor outer nuclear layers was significantly smaller for the CW lesions than the mode-locked lesions ( $p < 0.04$ , T-Test at RPE, and  $p < 0.001$ , T-Test at photoreceptor outer nuclear layer). The results are included in Table 12.

Chronic (2 months old), moderate-energy, 7.5-mJ (30 mW for 0.25 s) mode-locked and CW lesions were similar in appearance at the same energy without a significant difference in horizontal lesion size (Figure 18 A & B). Sections revealed loss of photoreceptor nuclei with a bowing outward of the external limiting membrane. There were minimal pyknotic nuclei and a focal site of disrupted photoreceptor outer segments, damaged RPE and choroidal damage. RPE cells and/or pigment containing macrophages usually had formed a second layer over the injury site and less commonly migrated into the outer retina (Figure 18 A & B). There was no visible outer plexiform damage in the chronic, moderate-energy lesions in either group.

The acute pattern of thermal injury is grossly similar for all exposure energies after CW and mode-locked laser treatment of the retina on comparison of fundus appearance, fluorescein angiograms and light micrographs. The extent of retinal and choroidal damage is similar to that seen in prior CW laser studies in which a thermal damage mechanism was implicated in retinal lesion formation [86], [87], [88]. Within this limited study there was no apparent risk of rupture of Bruch's membrane in acute, higher-energy, mode-locked lesions when compared to the CW lesions of similar energy.

We found a difference in horizontal lesion size and in pattern of injury to photoreceptor nuclei between matched lesions in the two groups. This raises the question of some unexpected aberrations in the beam delivered to the retina from either laser (despite the precautions to match the laser energy delivered) or of mechanisms of injury in addition to the thermal damage manifest in these lesions. Additional photochemical injury or photoreceptor nuclear damage from the mode-locked laser cannot be ruled out on the basis of this study. Konig et al. [89] reported a possible photochemical effect on mammalian cells specifically from mode-locked laser treatment. To resolve this question of effect, future biochemical studies of photoreceptor nuclei after application of mode-locked laser energy versus CW laser energy would be needed.

Reference	$\lambda$ (nm)	Exposure Duration (ms)	MVL Threshold (mJ)	$\frac{1}{4}$ - sec Normalized Threshold (mJ)	Exposure Site / Obs. Time (hrs)	Laser Exposure Type
[90]	488.0	200	1.80	2.13	Par / 24	CW
[54]	488.0	250	2.38	2.38	Mac / 1	CW
[90]	514.5	200	1.60	1.89	Par / 24	CW
[28]	514.5	1000	5.50	1.94	Par / 1	CW
[37]	514.5	125	1.40	2.35	Par / 1	CW
[91]	514.5	500	4.5	2.68	Mac / 24	CW
[66]	514.5	100	1.06	2.11	Mac / 1	CW
[66]	514.5	500	3.45	2.05	Mac / 1	CW
[92]	514.5	125	1.44	2.42	Mix / 1	CW
[93]	568.2	120	1.32	2.29	Par / 1	CW
[93]	568.2	500	3.90	2.32	Par / 1	CW
[29]	632.8	250	3.15	3.15	Par / 24	CW
[90]	632.8	200	2.20	2.60	Par / 24	CW
[90]	632.8	200	1.70	2.01	Mac / 24	CW
[94]	647.0	100	1.0	1.99	Mac / 1	CW
[81]	692.0	100	1.94	3.86	Par / 1	CW
[81]	694.4	100	1.7	3.38	Par / 1	CW
[81]	700.0	100	1.48	2.94	Par / 1	CW
[81]	709.8	100	2.23	4.43	Par / 1	CW
[81]	750.0	100	2.24	4.45	Par / 1	CW
[79]	755.0	100	2.47	4.91	Par / 1	CW
[81]	779.5	100	1.75	3.48	Par / 1	CW
[81]	789.0	100	2.17	4.31	Par / 1	CW
[81]	799.5	100	2.94	5.85	Par / 1	CW
[81]	810.2	100	3.81	7.57	Par / 1	CW
[81]	820.2	100	4.33	8.61	Par / 1	CW
[81]	830.2	100	3.12	6.20	Par / 1	CW
[81]	850.3	100	3.7	7.36	Par / 1	CW
[81]	857.0	100	3.54	7.04	Par / 1	CW
[80]	860.0	100	3.34	6.64	Par / 1	CW
[80]	870.0	100	3.64	7.24	Par / 1	CW
[80]	880.0	100	3.26	6.48	Par / 1	CW
[80]	890.0	100	4.49	8.93	Par / 1	CW
[80]	900.0	100	4.32	8.59	Par / 1	CW
[82]	912.0	100	5.66	11.25	Par / 1	CW
[82]	920.0	100	5.46	10.86	Par / 1	CW
[82]	930.0	100	5.32	10.58	Par / 1	CW
[82]	950.0	100	9.15	18.19	Par / 1	CW
[82]	970.0	100	14.1	28.03	Par / 1	CW
[82]	990.0	100	19.9	39.56	Par / 1	CW
[82]	1000	100	15.2	30.22	Par / 1	CW
[82]	1010	100	13.7	27.24	Par / 1	CW
[63]	1060	100	6.7	13.3	Mac / 1	CW
[84]	1060	150	16.5	24.2	Par / 0.1	CW
[67]	1064	500	26.5	15.8	Mac / 1	CW
[57]	590	200	2.95	3.49	Mac / 24	Pulsed
[85]	860	500	19.2	11.4	Par / 1	Pulsed
[85]	860	125	6.9	11.6	Par / 1	Pulsed
[83]	860	500	19.2	11.4	Mix / 1	Pulsed
[93]	1064	1000	64.8	22.9	Par / 1	Pulsed
This Study	800	250	5.77	5.77	Par / 24	CW
This Study	800	250	6.14	6.14	Par / 24	Mode-Locked

Table 11. Comparison of  $\frac{1}{4}$  - second exposure visible and near-infrared MVL thresholds.

Laser Power	Average Width of Continuous Wave Lesions in Microns (+/- standard deviation)		Average Width of Mode-Locked Lesions in Microns (+/- standard deviation)	
	Photoreceptor Nuclei*	Retinal Pigment Epithelium**	Photoreceptor Nuclei*	Retinal Pigment Epithelium**
38-40mW	7.5 ± 2.62	15 ± 3.42	13 ± 2.19	17 ± 3.64
45mW	7 ± 2.92	16.5 ± 2.82	16 ± 4.11	22 ± 1.25
50-51mW	12 ± 4.54	18.5 ± 6.90	18 ± 6.08	23 ± 7.16

\* Statistically significant difference between lesion width at photoreceptor outer nuclei ( $p < 0.001$ , T-Test)

\*\* Statistically significant difference between lesion width at RPE ( $p < 0.04$ , T-Test)

**Table 12.** Experimental results for acute (< one hour) histopathology –lesion size comparison.

## CONCLUSIONS

### Single Pulse Thresholds

We have evaluated the effects of near-infrared ultrashort laser pulses on the retinas of rhesus monkey eyes and performed threshold measurements for minimum visible lesions (MVLs) at pulse widths from nanosecond to femtoseconds.

Near-infrared single laser pulses were placed within the macular area of live rhesus monkey eyes for five different pulse widths (7 ns, 80 ps, 20 ps, 1 ps, and 150 fs). One visible wavelength at 530 nm at 100 fs was also included in this study. Visible lesion thresholds (MVL-ED<sub>50</sub>) were determined one hour after exposure and 24 hours after exposure. Fluorescein angiography (FAVL-ED<sub>50</sub>) thresholds were also determined using a probit analysis on the dosage. Thresholds were calculated as that dosage causing a 50 percent probability for damage and the fiducial limits were calculated at the 95 percent confidence level.

For all pulse widths, the 24-hour MVL-ED<sub>50</sub> threshold dose was lower than the one-hour threshold and they all decreased with decreasing pulse width. Thresholds at the one-hour reading decreased from 28.7  $\mu$ J for 7 ns to 1.8  $\mu$ J at 150 fs while the thresholds at 24 hours decreased from 19.1  $\mu$ J at 7 ns to 1.0  $\mu$ J at 150 fs. The doubled 1060 nm wavelength of 530 nm threshold decreased from 0.36  $\mu$ J to 0.16  $\mu$ J after 24 hours. Fluorescein angiography (FA) thresholds were very much higher than that for the visible lesion thresholds showing that FA was not as sensitive in determining damage levels.

Laser pulse widths below 1 ns in the near-infrared are capable of producing visible lesions in rhesus monkey eyes with pulse energies between 5  $\mu$ J and 1  $\mu$ J. Also, the near-infrared thresholds for these pulse widths are much higher than for the visible wavelengths. As with visible wavelengths, fluorescein angiography is not as sensitive in determining threshold levels as visually observing the retina through a fundus camera.

### Multiple Pulse Thresholds

There are several conclusions that may be drawn from our data regarding visible lesion thresholds due to multiple pulse lasers. Again, we found that the FA technique for determining lesion thresholds is not as sensitive as the direct ophthalmoscopic observation. This data confirmed all of our previous measurements within the primate eye.

We first measured the sensitivity differences between the macula and paramacula so that our results could be related to the macula for safety standard development. We found the ratio of the MVL thresholds of the near paramacula/macula (<10 degree visual angle) was 1.56 for these ultrashort laser pulses of near-IR and this ratio (paramacula/macula) compared favorably with other ratios reported for different wavelengths and pulse widths.

Another conclusion which may be drawn is that the visible lesion thresholds, for these 130 fs pulses at 800 nm, do not follow the ANSI Z136.1 standard for  $Q(n^{-1/4})$  reduction for multiple pulses that has been established for longer pulse widths. During the first 10 pulses of a repetitive pulse laser with a PRF of 1 kHz, the MVL threshold drops much faster than the  $(n^{-1/4})$  predicts (3.70 versus 1.78 predicted). The threshold remains nearly constant thereafter with only a 10 percent decrement for each decade increase in the number of pulses. We found a minimum pulse energy of 110 nJ/pulse for the damage threshold for pulse trains( 130 fs, 800 nm, 1 kHz) from 10 ms out to 10 seconds. Thus, it may be concluded for multiple pulse exposures greater than 10 pulses that there is a minimum pulse energy below which no visible damage will be observed within the fundus of the eye.

### **Macular vs. Paramacular Thresholds**

Single 130-femtosecond (fs) laser pulses in the near-IR (800 nm) were used to create ophthalmoscopically-viewed minimum visible lesions (MVL) within the macular and paramacular regions in rhesus monkey eyes. MVL thresholds at one hour and 24 hours are reported as the 50 percent probability for damage ( $ED_{50}$ ) together with their fiducial limits at the 95 percent confidence level. These measured thresholds are compared with previously reported thresholds for near-IR and visible wavelengths for both macular and paramacular areas. Threshold doses were lower at the 24-hour reading than at the one-hour reading for both retinal regions and the  $ED_{50}$ s for the macula were slightly lower than for the paramacula. We measured the 24-hour MVL  $ED_{50}$  thresholds to be 0.35  $\mu$ J and 0.55  $\mu$ J for the macular and paramacular areas, respectively. The combined data for both areas yielded a threshold of 0.44  $\mu$ J.

### **Retinal Image Size and Thresholds**

Our results show that as the retinal spot size increases, the radiant exposure necessary to cause an MVL decreases, but not in proportion to the retinal image area. This decreasing radiant exposure for increasing retinal spot sizes at 150 fs follows the trend shown previously for studies done from 30 picoseconds to 10 seconds. Thus, extended sources for 150 fs and 1060 nm show no deviation from the trend of decreasing radiant exposure for increasing retinal image sizes. We conclude that the current correction factors used in the laser safety standards also apply to femtosecond laser exposures between 400 nm and 1400 nm.

### **Mode-Locked vs. CW Thresholds**

Our data indicate that average power dictates the damage threshold for the 800-nm, 76-MHz mode-locked, 100-fs laser. This experiment has provided the most direct comparison of damage thresholds possible, with nearly identical beam propagation parameters for both laser exposures. These results point to a thermal damage mechanism as has been described in prior work with CW lasers. Although histopathology indicates that the acute pattern of thermal injury

is similar after CW and mode-locked laser treatment of the retina, this assessment of acute and short-term morphology does not rule out mechanisms of injury in addition to the thermal damage manifest in these lesions. The extent of retinal and choroidal damage and the extended outer plexiform damage is similar to that seen in prior CW laser studies in which a thermal damage mechanism was implicated in retinal lesion formation. The findings of comparable acute and chronic lesions at comparable laser energies from CW and femtosecond mode-locked laser delivery support the expectation of comparable gross clinical response to either treatment.

Within the parameters tested, it appears that a 76-MHz mode-locked femtosecond pulse trains produces effects quite similar to a CW exposure with the same laser duration as the femtosecond, multiple-pulse envelope. Laser delivery with the mode-locked system to produce visible retinal lesions results in an overall lesion comparable to that produced by a CW exposure. Raising and lowering the energy per fs pulse in the mode-locked train of pulses would not be expected to change this basically thermal injury effect until the peak power per individual fs pulse exceeded that required for laser induced breakdown. The level of energy required to reach laser induced breakdown in an eye from an 800 nm 100 fs pulse is quite high, 0.56  $\mu\text{J}$  per 100 fs pulse [38]. If this energy was incorporated into a 0.25 sec 76-MHz mode-locked pulse-train, the energy in the total pulse would be greater than 10 J or 1700 times the energy used to produce a retinal lesion in this study. This far exceeds parameters of laser energy that could possibly be used for ophthalmic treatment, as this is much greater energy than that at which severe thermal injury would already occur. Thus the incremental delivery of energy in 100 fs laser pulses within a pulse train may be useful for ophthalmic treatment without the worry of producing laser-induced breakdown, particularly as the pulse duration is reduced and the repetition rate is increased. In conclusion, we have shown experimentally equivalent retinal damage thresholds for quarter-second CW and mode-locked laser pulses at 800 nm with slight variations in histopathologic findings.

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# APPENDIX A

This appendix contains a comprehensive summary of the data collected and analysis results for the various experiments described in this report. For each threshold value reported, we have assembled the raw data collected, as well as the results of the probit analysis. Also provided is a graph illustrating the probit analysis results.

In order to understand these results, we have also prepared a brief summary of the probit analysis technique and a description of the data provided. This complete data set and description should allow future researchers to replicate our analysis results. It also allows for the application of alternate analysis techniques, depending upon the application of the data or needs for uncertainties to be determined to alternate confidence intervals.

## Probit Analysis Methods and Data Description

### Introduction

Probit analysis was developed to analyze discrete or dichotomous data including natural or threshold response rate for biological systems. This method is used as a statistical tool to determine the probability of dose-response curves for minimum visible lesions produced within the eye and in the skin for single laser pulses. In most cases the dose or laser pulse energy values required to produce a visible lesion within the eye is reported as the ED<sub>50</sub> dose or that dose which has a 50% probability of creating a visible lesion. However the complete probability curve is calculated during the iterative process and the printout generally gives points between 1% and 99%.

Graphical methods for the Probit analysis have been around for over 50 years and were used quite extensively because of their simplicity and ease of use. The data are plotted using this method; a straight line is drawn through the data points, and the ED<sub>50</sub> level is read from the graph. The slope of the straight line can also be determined from the graph. Later, a simplified graphical method was developed which included graph paper especially designed to permit rapid analysis. However all of these methods were developed before the modern day computer and therefore cannot compete with the speed or accuracy of computer derived exact solutions of the EZ-Probit procedure<sup>1</sup>.

### Methods

Most of the original development of the Probit method can be attributed to D.J.Finney<sup>2</sup> when he first published his book on Probit analyses in 1947. His procedure is the most widely used to analyze yes/no data and other discrete event data. Finney



developed the methods to utilize the Probit analyses but it still takes a computer program to process the data. All programs use the methods developed by Finney and utilize the exact Probit, iterative method.

The Probit procedure computes maximum-likelihood estimates of the slope and intercept of the Probit equation using a modified Newton-Raphson algorithm. The data set used by EZ-Probit must include either a response variable giving the level of response for each observation or a pair of variables giving the number of subjects tested and the number of subjects responding for each dose of the independent variable values. A goodness-of-fit Chi-square value is computed. Inverse confidence limits for one of the independent variables are calculated and the confidence limits are computed using a critical value of 1.96, which corresponds to an approximate 95 percent confidence interval. When the Pearson goodness of fit chi-square test is calculated and the p-value for the test is too small, variances and covariances are adjusted by a heterogeneity factor and a critical value from the t-distribution is used to compute the fiducial limits. The p-values used for the chi-square test can be set to different levels with a default p-value of 0.10. Also calculated and outputted is the slope of the Probit line between the ED<sub>84</sub> and the ED<sub>50</sub> values. One difference between Frisch<sup>3</sup> and the EZ-Probit is the way slope is defined. Frisch defines slope of the Probit as the ratio of ED<sub>84</sub> / ED<sub>50</sub> while EZ-Probit defines it as the slope of the straight line of best fit to the data. The two are inversely related and the slope of the Probit may be obtained from the ED<sub>84</sub> / ED<sub>50</sub> ratio simply by taking the reciprocal of the logarithm<sub>10</sub> of the ratio (ED<sub>84</sub> / ED<sub>50</sub>). About 2.5 is the crossover point of these two numbers and the theoretical minimum for the ratio is "1", i.e., the slope of the Probit would be infinite in this case.

The following formulas are used to calculate the energy dose for a given probability and the associated fiducial limits for that probability. Note that the Probit curve is calculated using the log<sub>10</sub> of the input energy values. Therefore the following formulas convert the Probit data back energy values by raising 10 to the power of the result.

Equation 1

$$E(x) = 10^{\left(\frac{A(x)-b}{\alpha}\right)}$$

In Equation 1, x is the probability of interest, E(x) is the dosage that will give that probability of effect, A(x) is the inverse log-normal distribution. The values α and b are the slope and intercept (0.5), respectively.

Additionally, the "fiducial limits" which describe the uncertainty in dosage required to provide a given probability of damage. These fiducial limits are determined for a certain percentage confidence interval. Equations which are used to determine the fiducial limits above and below E(x) can be summarized with the next four equations. In the data that we have assembled, this confidence is 95%, resulting in t value of 1.96. The value of g is



a weighting factor that is generated by the data analysis, along with SXX and S0 which come from a co-variance analysis of the data. The value of **b** is the slope of the data as reported.

Equation 2

$$B(E(x)) = \log[E(x)] + \frac{g * [\log(E(x)) * \bar{x}]}{(1 - g)}$$

Equation 3

$$\Delta = \frac{t}{\alpha * (1 - g)} + \sqrt{\frac{(1 - g)}{s0} + \frac{\{\log[E(x)] - \bar{x}\}^2}{SXX}}$$

Equation 4

$$FL_{upper} = 10^{B(E(x+\Delta))}$$

Equation 5

$$FL_{lower} = 10^{B(E(x-\Delta))}$$

Equation 6

$$g = \frac{t^t}{b^2 S_{xx}}$$

Equation 7

$$\frac{1}{S_0} = \frac{\left[ \frac{b(1 - g) \log(FL_{Upper}) - b(1 - g) \log(ED50) - b * g(\log(ED50) - \bar{x})}{t} \right]^2}{1 - g} - \frac{(\log(ED50) - \bar{x})^2}{S_{xx}}$$

EZ-Probit has the following printout and each of the terms will be defined as per Finney. Since the EZ-Probit followed Finney exactly in carrying out the computational steps on the computer, all parameters are exactly as defined by Finney. The reader is referred to the Finney's book<sup>2</sup> "Probit Analysis" for a complete explanations of the procedures used in the probit analysis.

## References

1. Cain, C. P., G. D. Noojin and L. Manning, "A Comparison of Various Probit Methods for Analyzing Yes/No Data on a Log Scale," AL/OR-TR-1996-0102 (1996).
2. Finney, D.J., Probit Analysis, 3rd edition, Cambridge Univ. Press. 1971
3. Frisch, G. D., Quantal Response Analysis, Memo. Report M70-27-1 of Joint AMRDC-AMC Laser Safety Team, US Army, Frankfort Arsenal, Phil. PA, 19137, Aug. 1970.

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Tue Oct 08 10:26:31 2002

Input File

ONES = 28

ZEROES = 44

TOTAL = 72

Percent confidence = 0.95

ED50 = 85.2

Upper FL = 88.4

Lower FL = 82.6

Intercept = -100.

Slope = 51.9

Pearson's Chi-Sq = 30.2651

Probability of Chi-Sq = 0.9995

h = 1.00 g = 0.43 t = 1.96

Log XBAR = 1.93 Log YBAR = 4.90

SYX = 39.170

SXY = 0.171

SXX = 0.003

S0 = 11.715

Iterations = 20

DF = 61

FL	Prob	Dose	Lower FL	Upper FL	Prob	Dose	Lower FL	Upper
	0.01	76.9	63.3	80.3	0.55	85.7	83.3	89.4
	0.02	77.8	65.5	81.0	0.60	86.2	83.9	90.6
	0.03	78.4	67.0	81.4	0.65	86.7	84.5	91.8
	0.04	78.8	68.1	81.7	0.70	87.2	85.0	93.3
	0.05	79.2	69.0	82.0	0.75	87.8	85.5	94.9
	0.06	79.5	69.8	82.2	0.80	88.4	86.1	96.8
	0.07	79.8	70.5	82.4	0.85	89.2	86.7	99.1
	0.08	80.1	71.1	82.6	0.90	90.2	87.4	102.
	0.09	80.3	71.6	82.8	0.91	90.4	87.5	103.
	0.10	80.5	72.2	82.9	0.92	90.7	87.7	104.
	0.15	81.4	74.3	83.6	0.93	91.0	87.9	105.
	0.20	82.1	76.1	84.2	0.94	91.3	88.1	106.
	0.25	82.7	77.5	84.8	0.95	91.7	88.4	107.
	0.30	83.3	78.8	85.4	0.96	92.1	88.6	108.
	0.35	83.8	80.0	86.1	0.97	92.6	89.0	110.
	0.40	84.3	81.0	86.8	0.98	93.3	89.4	113.
	0.45	84.7	81.8	87.6	0.99	94.5	90.1	117.
	0.50	85.2	82.6	88.4				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
28.4	1	0	73.3	1	0	88.1	1	1
31.9	1	0	73.6	1	0	91.4	1	1
34.5	1	0	74.1	1	0	91.9	1	1
38.2	1	0	74.8	1	0	92.1	1	1
41.7	1	0	75.8	1	0	93.6	1	1
45.6	1	0	76.2	1	0	96.7	1	1
48.3	1	0	77.7	1	0	97.7	1	1
52.4	1	0	78.4	1	0	99.6	1	1
52.7	1	0	78.6	1	0	102.	1	1
53.3	2	0	79.4	1	1	105.	1	1
54.8	1	0	81.5	1	0	106.	1	1
57.9	1	0	81.8	2	0	122.	1	1
59.4	1	0	82.5	2	0	123.	1	1
61.3	1	0	83.0	1	0	124.	2	2
64.2	1	0	83.2	2	0	125.	1	1
65.1	1	0	85.6	1	1	126.	1	1
67.3	2	0	85.9	3	3	130.	1	1
69.0	1	0	86.1	1	0	131.	1	1
69.5	2	0	86.6	1	1	136.	1	1
70.2	1	0	87.1	2	0	137.	1	1
71.7	1	0	87.3	1	1			
Totals							72	28

In this example, the input data file contained 72 data points with 28 ones and 44 zeroes. The fiducial limits were calculated at their 95% confidence level as printed out for the upper and lower FLs. The ED50 is shown to be 85.2 which is also shown in the next table for the 0.50 Prob and Dose at the bottom of the table. This 85.2 is calculated from the (Log XBAR = 1.93) as the antilog(base 10) of 1.93. The hprintout shows that the line with the best fit to the data is a line with an intercept of (minus) -100 and with a slope of 51.9. This slope would be the equivalent to Frisch's slope of 1.08, which is very close to 1.0.

The use of Pearson's Chi-square test as a measure of the discrepancy between the observations and the predictions increases the confidence in the data and allows one to see how close the predictions fit the data or the goodness of fit. The Chi-sq is the weighted sum of squares of the difference between the empirical and weighted probits or:

**Equation 8**  $\text{Chi-sq} = \chi^2 = \text{Syy} - \text{Sxy}^2/\text{Sxx}$

The S-values given in the above analyses gives  $\chi^2 = 39.17 - (0.171)^2/0.003 = 30.265$  as shown in the above calculations. These S-values were obtained after 20 iterations of calculating the probit line, using the new values to calculate a new probit line, etc. until the error was minimized. The S0 is introduced as a weighting factor is calculating the working probits at each dose to arrive at the adjusted estimates. The Xbar and Ybar are then calculated as the weighted linear regression of y on x, the weighting factor being S0.

The  $h = 1.00$  value is a measure of the heterogeneity of the data and the  $\chi^2$  test for heterogeneity of discrepancies between observed and expected numbers is valid only when the expected numbers are not small. This heterogeneity factor:

**Equation 9**  $h = \chi^2/(k-2)$

can be regarded as a factor estimating by which all weights have been overestimated. All variances can then be multiplied by h to arrive at new values based on (k-2) degrees of freedom. In all uses of standard errors, the t-distribution with (k-2) degrees of freedom will then be used instead of the normal distribution. This amounts to empirical assessment of standard errors and admission of a wider range of values as within the limits of experimental error. In general h will equal 1 and no adjustments will be necessary.

Two tables are printed with the output data, the first gives the doses required for probabilities from 1 percent to 99 percent throughout the ranges. The second table orders the data by doses from smallest to largest and the attempts at each dose along with the hits at that dose as a one (1) or a zero(0).

**IR Study (7ns) - MVL - 1-Hour**  
987 OD, 995 OS, 997 OS

ONES = 33 ZEROES = 36 TOTAL = 69

Percent confidence = 0.95

ED50 = 28.7 Upper FL = 39.1 Lower FL = 22.2

Intercept = -4.79 Slope = 3.29

Pearson's Chi-Sq = 50.0694 Probability of Chi-Sq = 0.8400

h = 1.00 g = 0.21 t = 1.96

Log XBAR = 1.41 Log YBAR = 4.85

SYX = 68.022 SXY = 5.460 SXX = 1.661 S0 = 31.458

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	5.63	1.45	9.51	0.55	31.3	24.5	44.4
0.02	6.81	2.06	10.9	0.60	34.3	26.8	51.0
0.03	7.69	2.57	11.9	0.65	37.6	29.2	59.2
0.04	8.42	3.03	12.7	0.70	41.4	31.9	69.6
0.05	9.07	3.46	13.4	0.75	46.0	34.8	83.3
0.06	9.66	3.88	14.0	0.80	51.7	38.2	102.
0.07	10.2	4.29	14.6	0.85	59.3	42.4	130.
0.08	10.7	4.69	15.2	0.90	70.4	48.3	177.
0.09	11.2	5.08	15.7	0.91	73.4	49.8	191.
0.10	11.7	5.47	16.2	0.92	76.8	51.4	207.
0.15	13.9	7.40	18.6	0.93	80.7	53.3	226.
0.20	15.9	9.36	20.8	0.94	85.3	55.5	250.
0.25	17.9	11.4	23.0	0.95	90.8	58.1	281.
0.30	19.9	13.5	25.4	0.96	97.8	61.3	322.
0.35	21.9	15.6	28.1	0.97	107.	65.4	380.
0.40	24.0	17.8	31.1	0.98	121.	71.3	474.
0.45	26.3	20.0	34.8	0.99	146.	81.6	674.
0.50	28.7	22.2	39.1				

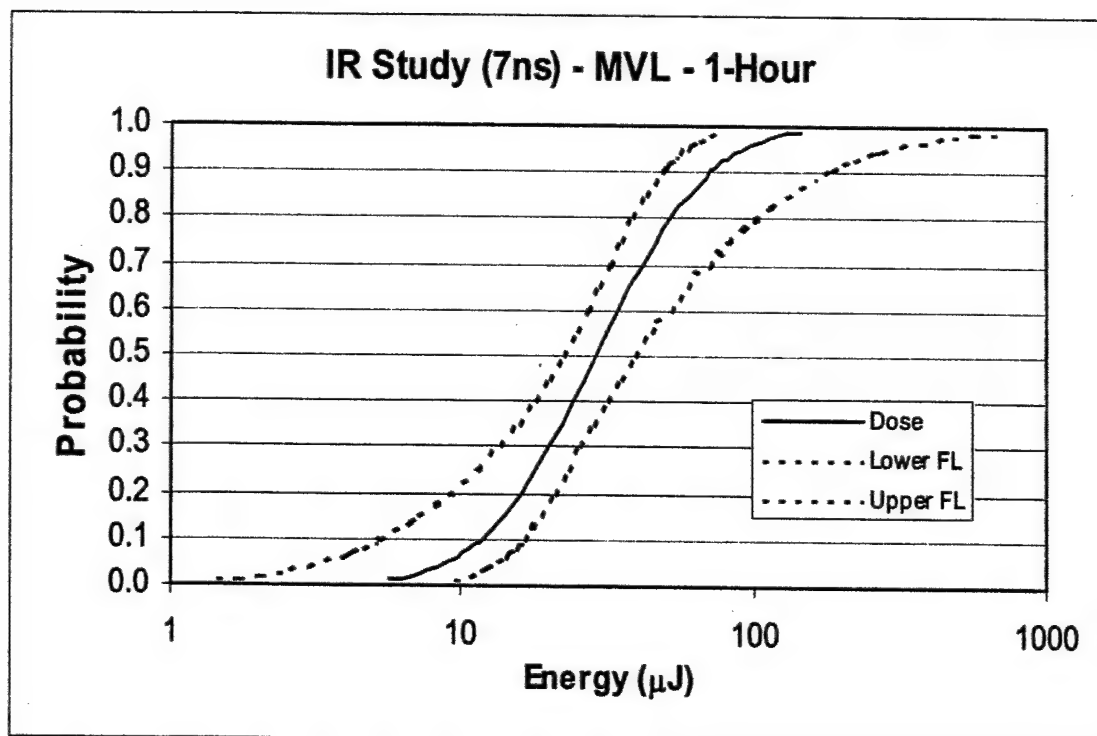
Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
8.90	1	0	20.6	1	0	37.2	1	0
9.00	2	0	21.4	1	0	37.9	1	1
9.20	1	0	21.7	1	0	38.7	1	1
9.60	1	0	22.5	1	1	39.4	1	0
10.8	1	0	22.7	1	0	42.7	1	0

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
11.6	1	0	23.5	2	1	42.8	1	1
12.5	1	0	23.9	1	0	44.6	1	1
12.8	2	1	24.8	1	0	45.1	1	1
13.0	1	0	25.0	1	1	46.4	1	1
13.5	1	0	27.0	1	1	48.7	1	0
13.7	1	1	27.5	1	0	77.4	1	1
13.8	2	0	29.4	1	1	84.0	1	1
14.2	1	0	31.0	2	2	101.	1	1
14.8	1	0	32.3	1	1	123.	1	1
15.3	1	1	32.5	1	1	126.	1	1
16.2	1	0	33.2	1	1	129.	1	1
16.6	1	0	33.7	1	1	143.	1	1
16.8	1	0	34.3	1	0	145.	1	1
17.6	1	0	35.6	1	0	152.	1	1
19.3	1	0	35.8	1	0	177.	1	1
20.5	1	1	36.4	2	1	188.	1	1

Totals

69

33



**IR Study (7ns) -MVL - 24-Hour**  
987 OD, 995 OS, 997 OS

ONES = 44 ZEROES = 25 TOTAL = 69

Percent confidence = 0.95

ED50 = 19.1 Upper FL = 24.4 Lower FL = 13.6

Intercept = -4.28 Slope = 3.35

Pearson's Chi-Sq = 51.3404 Probability of Chi-Sq = 0.8063

h = 1.00 g = 0.24 t = 1.96

Log XBAR = 1.34 Log YBAR = 5.19

SYX = 67.155 SXY = 4.728 SXX = 1.413 S0 = 30.876

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	3.84	0.688	7.05	0.55	20.8	15.4	27.1
0.02	4.63	0.991	8.02	0.60	22.7	17.4	30.4
0.03	5.22	1.25	8.72	0.65	24.8	19.3	34.7
0.04	5.71	1.49	9.28	0.70	27.3	21.4	40.3
0.05	6.14	1.71	9.77	0.75	30.3	23.7	47.9
0.06	6.53	1.93	10.2	0.80	34.0	26.2	58.6
0.07	6.90	2.15	10.6	0.85	38.9	29.3	74.8
0.08	7.24	2.36	11.0	0.90	46.0	33.4	103.
0.09	7.57	2.57	11.3	0.91	47.9	34.4	111.
0.10	7.89	2.78	11.7	0.92	50.1	35.6	120.
0.15	9.33	3.83	13.2	0.93	52.6	36.9	132.
0.20	10.7	4.94	14.6	0.94	55.5	38.4	147.
0.25	12.0	6.12	16.0	0.95	59.1	40.1	165.
0.30	13.3	7.40	17.4	0.96	63.6	42.3	190.
0.35	14.6	8.78	18.8	0.97	69.5	45.1	226.
0.40	16.0	10.3	20.4	0.98	78.3	49.0	284.
0.45	17.5	11.9	22.3	0.99	94.5	55.9	409.
0.50	19.1	13.6	24.4				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
8.90	1	0	20.6	1	0	37.2	1	0
9.00	2	0	21.4	1	0	37.9	1	1
9.20	1	0	21.7	1	0	38.7	1	1
9.60	1	0	22.5	1	1	39.4	1	1
10.8	1	1	22.7	1	1	42.7	1	1

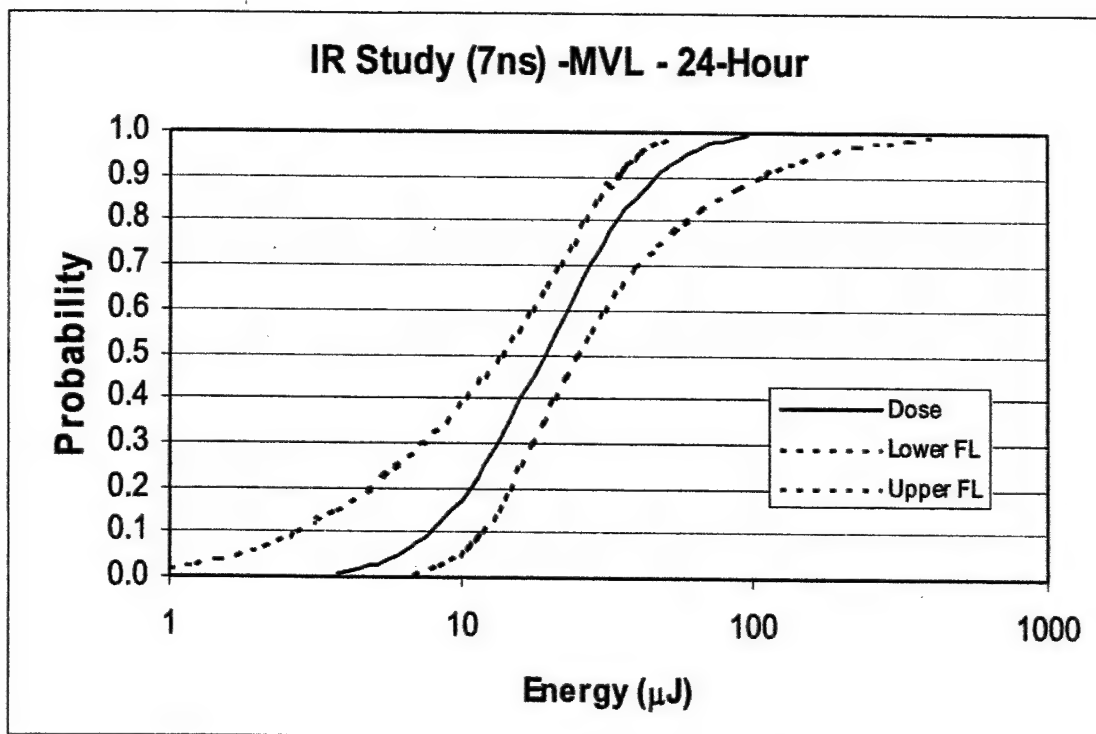


Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
11.6	1	0	23.5	2	1	42.8	1	1
12.5	1	0	23.9	1	1	44.6	1	1
12.8	2	1	24.8	1	1	45.1	1	0
13.0	1	0	25.0	1	1	46.4	1	1
13.5	1	0	27.0	1	1	48.7	1	1
13.7	1	1	27.5	1	0	77.4	1	1
13.8	2	2	29.4	1	0	84.0	1	1
14.2	1	0	31.0	2	1	101.	1	1
14.8	1	0	32.3	1	1	123.	1	1
15.3	1	0	32.5	1	1	126.	1	1
16.2	1	1	33.2	1	1	129.	1	1
16.6	1	1	33.7	1	1	143.	1	1
16.8	1	0	34.3	1	1	145.	1	1
17.6	1	0	35.6	1	1	152.	1	1
19.3	1	0	35.8	1	1	177.	1	1
20.5	1	1	36.4	2	2	188.	1	1

Totals

69

44



**IR Study (7ns) - FAVL - 1-Hour**

987 OD, 995 OS, 997 OS

ONES = 18 ZEROES = 51 TOTAL = 69

Percent confidence = 0.95

ED50 = 54.4 Upper FL = 87.4 Lower FL = 41.0

Intercept = -5.75 Slope = 3.31

Pearson's Chi-Sq = 50.9341 Probability of Chi-Sq = 0.8174

h = 1.00 g = 0.20 t = 1.96

Log XBAR = 1.56 Log YBAR = 4.43

SYY = 70.513 SXY = 5.909 SXX = 1.784 S0 = 24.067

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	10.8	3.81	16.8	0.55	59.4	44.4	100.
0.02	13.1	5.30	19.4	0.60	64.9	48.0	116.
0.03	14.7	6.52	21.3	0.65	71.1	51.8	135.
0.04	16.1	7.61	22.8	0.70	78.3	56.0	158.
0.05	17.3	8.62	24.2	0.75	86.9	60.8	189.
0.06	18.5	9.57	25.5	0.80	97.6	66.6	231.
0.07	19.5	10.5	26.6	0.85	112.	73.8	292.
0.08	20.5	11.4	27.8	0.90	133.	83.7	393.
0.09	21.4	12.2	28.8	0.91	138.	86.3	422.
0.10	22.3	13.1	29.9	0.92	144.	89.2	456.
0.15	26.5	17.1	35.0	0.93	152.	92.5	497.
0.20	30.3	20.9	40.1	0.94	160.	96.3	548.
0.25	34.0	24.4	45.7	0.95	171.	101.	612.
0.30	37.8	27.9	51.9	0.96	184.	106.	696.
0.35	41.6	31.2	58.9	0.97	201.	113.	817.
0.40	45.6	34.5	67.0	0.98	227.	124.	1.01e+003
0.45	49.8	37.7	76.4	0.99	274.	142.	1.41e+003
0.50	54.4	41.0	87.4				

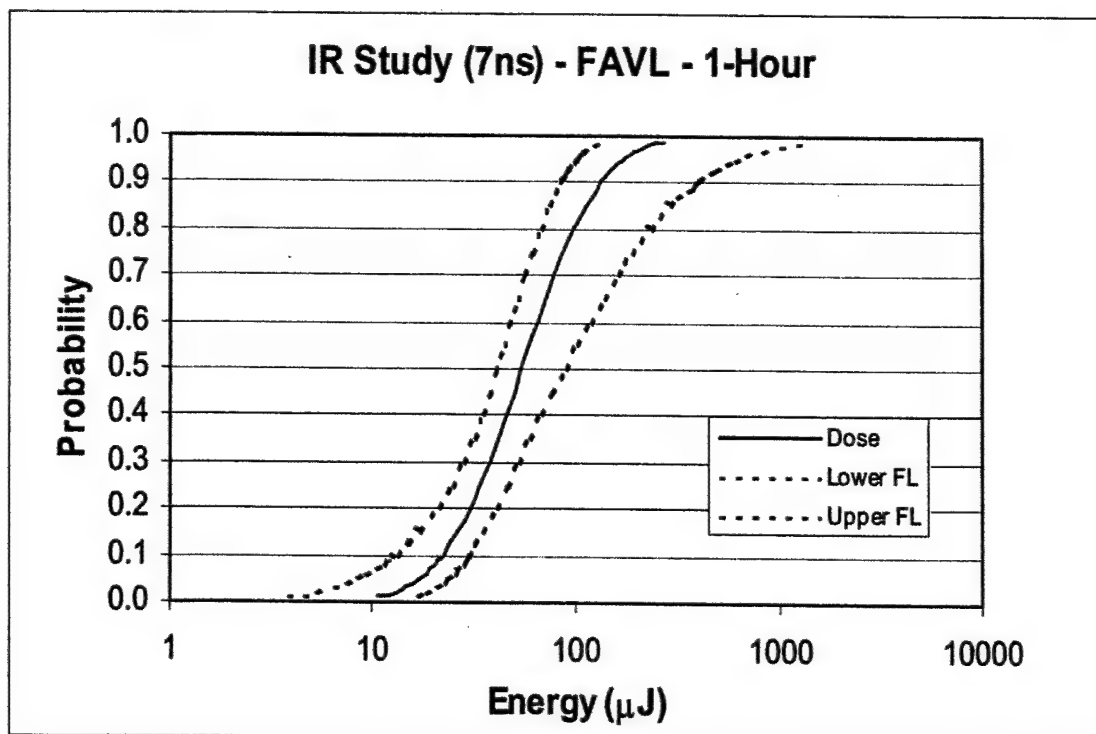
Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
8.90	1	0	20.6	1	0	37.2	1	0
9.00	2	0	21.4	1	0	37.9	1	1
9.20	1	0	21.7	1	0	38.7	1	0
9.60	1	0	22.5	1	0	39.4	1	1
10.8	1	0	22.7	1	0	42.7	1	0

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
11.6	1	0	23.5	2	2	42.8	1	0
12.5	1	0	23.9	1	0	44.6	1	0
12.8	2	0	24.8	1	0	45.1	1	1
13.0	1	0	25.0	1	0	46.4	1	0
13.5	1	0	27.0	1	1	48.7	1	0
13.7	1	0	27.5	1	0	77.4	1	0
13.8	2	0	29.4	1	0	84.0	1	0
14.2	1	0	31.0	2	0	101.	1	1
14.8	1	0	32.3	1	0	123.	1	1
15.3	1	0	32.5	1	1	126.	1	1
16.2	1	0	33.2	1	1	129.	1	1
16.6	1	0	33.7	1	0	143.	1	1
16.8	1	0	34.3	1	0	145.	1	1
17.6	1	0	35.6	1	0	152.	1	1
19.3	1	0	35.8	1	1	177.	1	1
20.5	1	0	36.4	2	0	188.	1	1

Totals

69

18



**IR Study (7ns) - FAVL - 24-Hour**  
987 OD, 995 OS, 997 OS

ONES = 13 ZEROES = 56 TOTAL = 69

Percent confidence = 0.95

ED50 = 57.6 Upper FL = 104. Lower FL = 46.5

Intercept = -13.5 Slope = 7.68

Pearson's Chi-Sq = 16.6663 Probability of Chi-Sq = 1.0000

h = 1.00 g = 0.41 t = 1.96

Log XBAR = 1.64 Log YBAR = 4.10

SYX = 26.049 SXY = 1.222 SXX = 0.159 S0 = 7.728

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	28.7	12.5	36.6	0.55	59.9	48.1	114.
0.02	31.1	15.4	39.0	0.60	62.2	49.6	126.
0.03	32.8	17.6	40.7	0.65	64.7	51.3	140.
0.04	34.1	19.4	42.2	0.70	67.5	52.9	156.
0.05	35.2	20.9	43.5	0.75	70.6	54.8	175.
0.06	36.2	22.3	44.7	0.80	74.2	56.8	200.
0.07	37.0	23.6	45.8	0.85	78.7	59.2	234.
0.08	37.8	24.7	46.9	0.90	84.7	62.3	285.
0.09	38.6	25.8	48.0	0.91	86.2	63.0	299.
0.10	39.2	26.8	49.0	0.92	87.8	63.9	315.
0.15	42.2	31.1	54.3	0.93	89.7	64.8	334.
0.20	44.8	34.4	59.8	0.94	91.9	65.8	356.
0.25	47.1	37.1	65.6	0.95	94.4	67.0	383.
0.30	49.3	39.4	72.0	0.96	97.4	68.4	418.
0.35	51.3	41.4	78.9	0.97	101.	70.2	465.
0.40	53.4	43.2	86.5	0.98	107.	72.6	536.
0.45	55.5	44.9	94.7	0.99	116.	76.6	670.
0.50	57.6	46.5	104.				

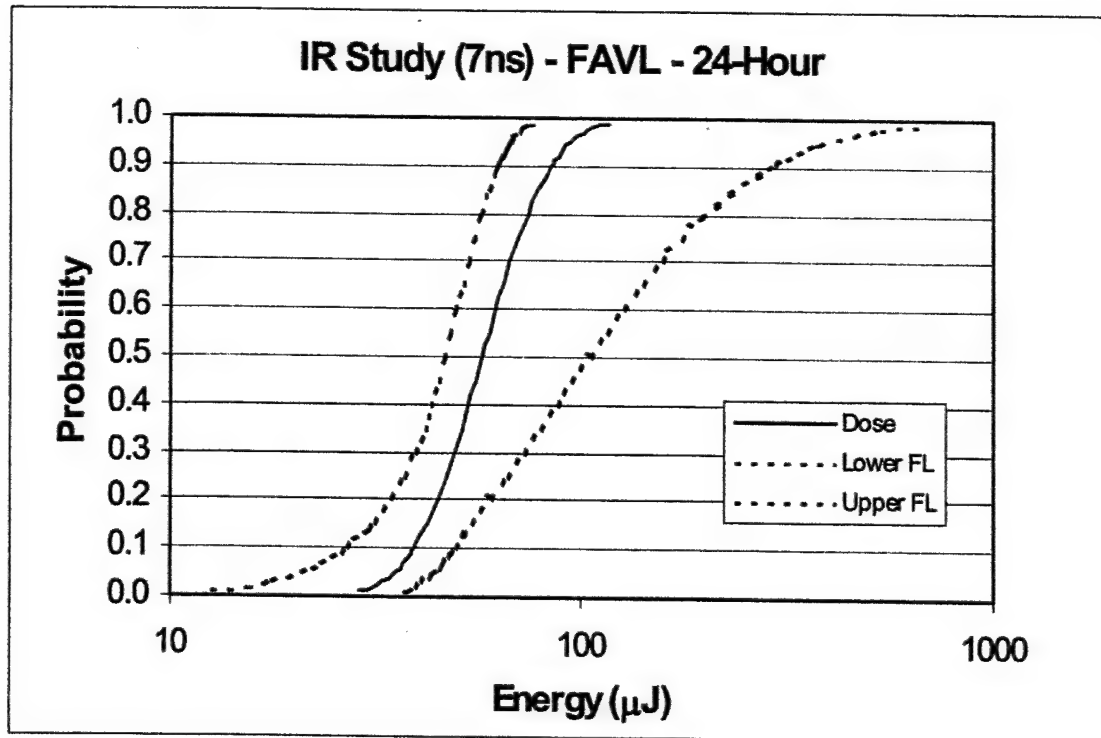
Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
8.90	1	0	20.6	1	0	37.2	1	0
9.00	2	0	21.4	1	0	37.9	1	0
9.20	1	0	21.7	1	0	38.7	1	0
9.60	1	0	22.5	1	0	39.4	1	0
10.8	1	0	22.7	1	0	42.7	1	0

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
11.6	1	0	23.5	2	0	42.8	1	0
12.5	1	0	23.9	1	0	44.6	1	1
12.8	2	0	24.8	1	0	45.1	1	0
13.0	1	0	25.0	1	0	46.4	1	1
13.5	1	0	27.0	1	0	48.7	1	1
13.7	1	0	27.5	1	0	77.4	1	0
13.8	2	0	29.4	1	0	84.0	1	1
14.2	1	0	31.0	2	0	101.	1	1
14.8	1	0	32.3	1	0	123.	1	1
15.3	1	0	32.5	1	0	126.	1	1
16.2	1	0	33.2	1	0	129.	1	1
16.6	1	0	33.7	1	0	143.	1	1
16.8	1	0	34.3	1	0	145.	1	1
17.6	1	0	35.6	1	0	152.	1	1
19.3	1	0	35.8	1	0	177.	1	1
20.5	1	0	36.4	2	0	188.	1	1

Totals

69

13



**IR Study (80ps) - MVL - 1-Hour**  
963 OD, 987 OS, A35 OD, A47 OS, A13 OD

ONES = 38 ZEROES = 62 TOTAL = 100

Percent confidence = 0.95

ED50 = 8.09 Upper FL = 15.5 Lower FL = 5.15

Intercept = -1.26 Slope = 1.38

Pearson's Chi-Sq = 91.8270 Probability of Chi-Sq = 0.4855

h = 1.00 g = 0.18 t = 1.96

Log XBAR = 0.718 Log YBAR = 4.74

SY Y = 112.603 SXY = 15.030 SXX = 10.874 S0 = 52.036

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.168	0.0117	0.505	0.55	9.98	6.30	21.2
0.02	0.264	0.0258	0.701	0.60	12.3	7.63	29.5
0.03	0.353	0.0424	0.864	0.65	15.4	9.20	42.0
0.04	0.438	0.0615	1.01	0.70	19.4	11.1	61.3
0.05	0.523	0.0833	1.15	0.75	24.9	13.5	93.0
0.06	0.607	0.108	1.29	0.80	32.9	16.7	149.
0.07	0.693	0.135	1.42	0.85	45.5	21.4	259.
0.08	0.779	0.165	1.55	0.90	68.4	28.9	521.
0.09	0.867	0.198	1.69	0.91	75.5	31.0	618.
0.10	0.957	0.233	1.82	0.92	84.1	33.5	743.
0.15	1.44	0.462	2.50	0.93	94.6	36.5	911.
0.20	1.99	0.784	3.27	0.94	108.	40.2	1.14e+003
0.25	2.63	1.21	4.18	0.95	125.	44.8	1.48e+003
0.30	3.38	1.76	5.31	0.96	150.	50.9	2.01e+003
0.35	4.26	2.44	6.79	0.97	186.	59.4	2.93e+003
0.40	5.31	3.23	8.79	0.98	248.	73.0	4.84e+003
0.45	6.56	4.13	11.6	0.99	390.	101.	1.07e+004
0.50	8.09	5.15	15.5				

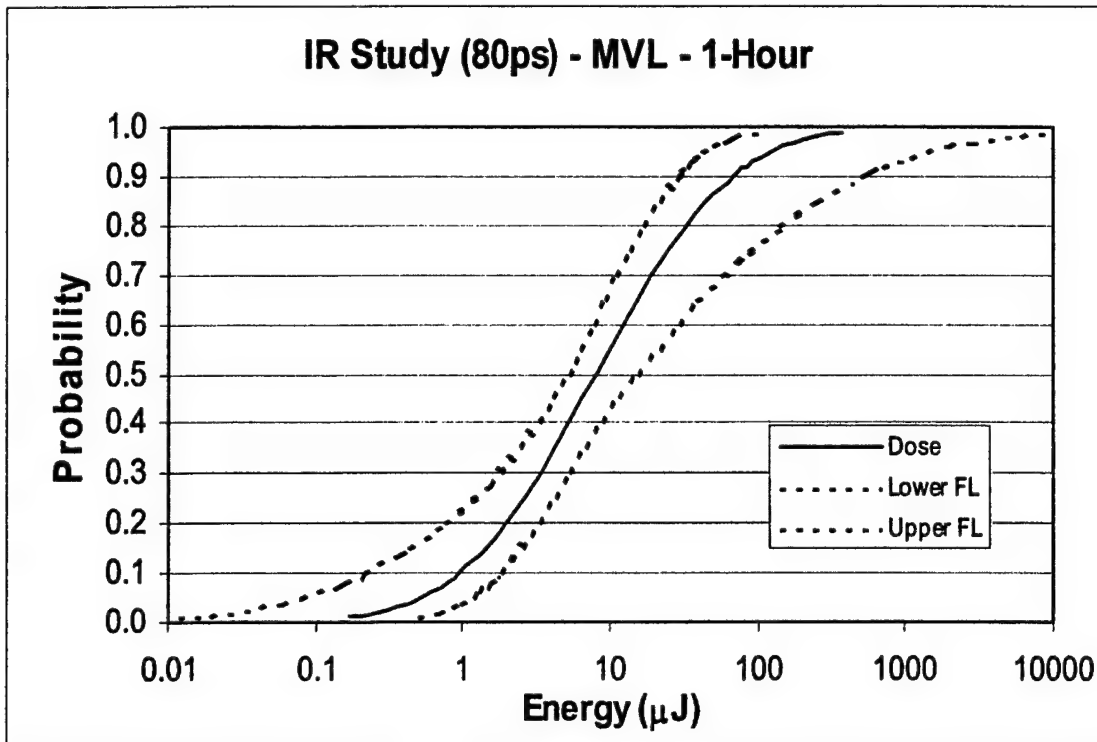
Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.450	1	0	2.60	1	0	8.80	1	0
0.540	1	0	2.63	1	0	9.00	1	0
0.600	2	0	2.69	1	0	9.10	1	0
0.720	1	0	2.70	1	0	9.30	1	0
0.770	1	0	2.77	1	0	9.40	1	0

<b>Dose</b>	<b>Tries</b>	<b>Hits</b>	<b>Dose</b>	<b>Tries</b>	<b>Hits</b>	<b>Dose</b>	<b>Tries</b>	<b>Hits</b>
0.830	1	0	2.87	1	0	9.49	1	1
0.900	1	0	3.15	1	0	9.85	1	0
1.00	1	0	3.34	1	0	10.2	1	1
1.06	1	0	3.44	1	0	10.3	1	1
1.10	2	0	3.50	1	0	11.0	1	0
1.13	2	2	3.53	1	1	11.2	1	0
1.15	1	0	3.90	1	1	11.6	2	1
1.20	2	1	3.94	1	0	11.7	1	1
1.27	1	0	4.00	1	1	12.2	1	0
1.30	1	1	5.00	1	0	14.9	1	1
1.36	1	0	5.21	1	1	17.4	1	0
1.38	1	0	5.24	1	1	18.2	1	1
1.43	1	1	5.74	1	0	19.0	1	1
1.53	1	0	5.85	1	1	21.0	1	1
1.56	1	0	6.04	1	1	22.6	1	1
1.84	1	0	6.19	1	1	25.7	1	1
1.88	1	1	6.23	1	0	27.0	1	1
1.90	1	1	6.30	1	1	32.6	1	1
1.95	1	0	6.52	1	0	36.8	1	1
2.05	1	0	6.90	1	0	37.0	1	1
2.12	1	0	7.13	1	0	38.0	1	1
2.30	1	0	7.14	1	0	40.0	1	1
2.34	1	0	7.17	1	0	40.3	1	1
2.42	1	0	7.53	1	0	51.0	1	1
2.49	1	0	7.80	1	1	53.6	1	1
2.50	1	0	7.87	1	0			
2.53	1	0	8.25	2	1			

**Totals**

**100 38**





**IR Study (80ps) -MVL - 24-Hour**

963 OD, 987 OS, A35 OD, A47 OS, A13 OD

ONES = 51 ZEROES = 49 TOTAL = 100

Percent confidence = 0.95

ED50 = 4.16 Upper FL = 5.77 Lower FL = 3.00

Intercept = -1.37 Slope = 2.21

Pearson's Chi-Sq = 81.8670 Probability of Chi-Sq = 0.7663

h = 1.00 g = 0.12 t = 1.96

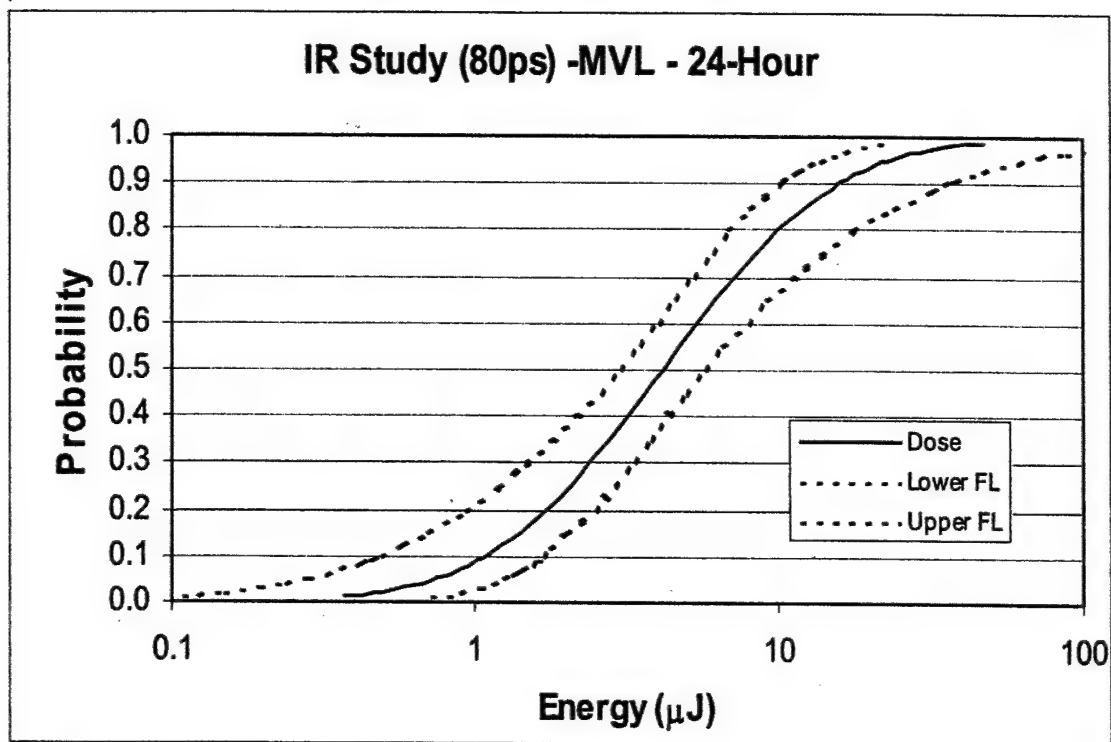
Log XBAR = 0.618 Log YBAR = 5.00

SYY = 114.005 SXY = 14.545 SXX = 6.582 S0 = 44.200

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.368	0.0969	0.724	0.55	4.74	3.46	6.72
0.02	0.489	0.149	0.901	0.60	5.41	3.98	7.91
0.03	0.585	0.195	1.04	0.65	6.21	4.56	9.44
0.04	0.670	0.238	1.15	0.70	7.18	5.23	11.4
0.05	0.749	0.281	1.25	0.75	8.39	6.02	14.2
0.06	0.822	0.323	1.35	0.80	9.99	6.99	18.1
0.07	0.893	0.365	1.44	0.85	12.2	8.29	24.2
0.08	0.961	0.407	1.53	0.90	15.8	10.2	35.2
0.09	1.03	0.449	1.61	0.91	16.8	10.7	38.5
0.10	1.09	0.492	1.69	0.92	18.0	11.3	42.5
0.15	1.41	0.714	2.08	0.93	19.3	12.0	47.4
0.20	1.73	0.955	2.47	0.94	21.0	12.8	53.6
0.25	2.06	1.22	2.87	0.95	23.1	13.8	61.6
0.30	2.41	1.51	3.30	0.96	25.8	15.0	72.6
0.35	2.78	1.83	3.79	0.97	29.5	16.7	88.9
0.40	3.19	2.19	4.34	0.98	35.3	19.2	117.
0.45	3.65	2.57	4.99	0.99	46.9	23.8	179.
0.50	4.16	3.00	5.77				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.450	1	0	2.60	1	0	8.80	1	0
0.540	1	0	2.63	1	0	9.00	1	1
0.600	2	0	2.69	1	0	9.10	1	0
0.720	1	0	2.70	1	0	9.30	1	0
0.770	1	0	2.77	1	0	9.40	1	1

<b>Dose</b>	<b>Tries</b>	<b>Hits</b>	<b>Dose</b>	<b>Tries</b>	<b>Hits</b>	<b>Dose</b>	<b>Tries</b>	<b>Hits</b>
0.830	1	0	2.87	1	0	9.49	1	1
0.900	1	0	3.15	1	0	9.85	1	1
1.00	1	1	3.34	1	0	10.2	1	1
1.06	1	0	3.44	1	0	10.3	1	1
1.10	2	0	3.50	1	0	11.0	1	0
1.13	2	1	3.53	1	1	11.2	1	1
1.15	1	0	3.90	1	1	11.6	2	1
1.20	2	0	3.94	1	0	11.7	1	1
1.27	1	0	4.00	1	1	12.2	1	1
1.30	1	0	5.00	1	1	14.9	1	1
1.36	1	0	5.21	1	1	17.4	1	1
1.38	1	0	5.24	1	0	18.2	1	1
1.43	1	1	5.74	1	0	19.0	1	1
1.53	1	0	5.85	1	1	21.0	1	1
1.56	1	0	6.04	1	1	22.6	1	1
1.84	1	0	6.19	1	1	25.7	1	1
1.88	1	1	6.23	1	1	27.0	1	1
1.90	1	1	6.30	1	1	32.6	1	1
1.95	1	0	6.52	1	1	36.8	1	1
2.05	1	0	6.90	1	1	37.0	1	1
2.12	1	1	7.13	1	0	38.0	1	1
2.30	1	0	7.14	1	1	40.0	1	1
2.34	1	1	7.17	1	0	40.3	1	1
2.42	1	0	7.53	1	1	51.0	1	1
2.49	1	0	7.80	1	1	53.6	1	1
2.50	1	0	7.87	1	1			
2.53	1	0	8.25	2	2			
<b>Totals</b>							<b>100</b>	<b>51</b>



**IR Study (80ps) - FAVL - 1-Hour**  
963 OD, 987 OS, A35 OD, A47 OS, A13 OD

ONES =19      ZEROES = 81      TOTAL = 100

Percent confidence = 0.95

ED50 = 14.3    Upper FL = 22.0      Lower FL = 10.8

Intercept = -4.75      Slope = 4.11

Pearson's Chi-Sq = 113.2627    Probability of Chi-Sq = 0.0656

h = 1.23      g = 0.24      t = 1.99

Log XBAR = 1.04    Log YBAR = 4.55

SYX = 133.154      SXY = 4.836    SXX = 1.176    S0 = 20.484

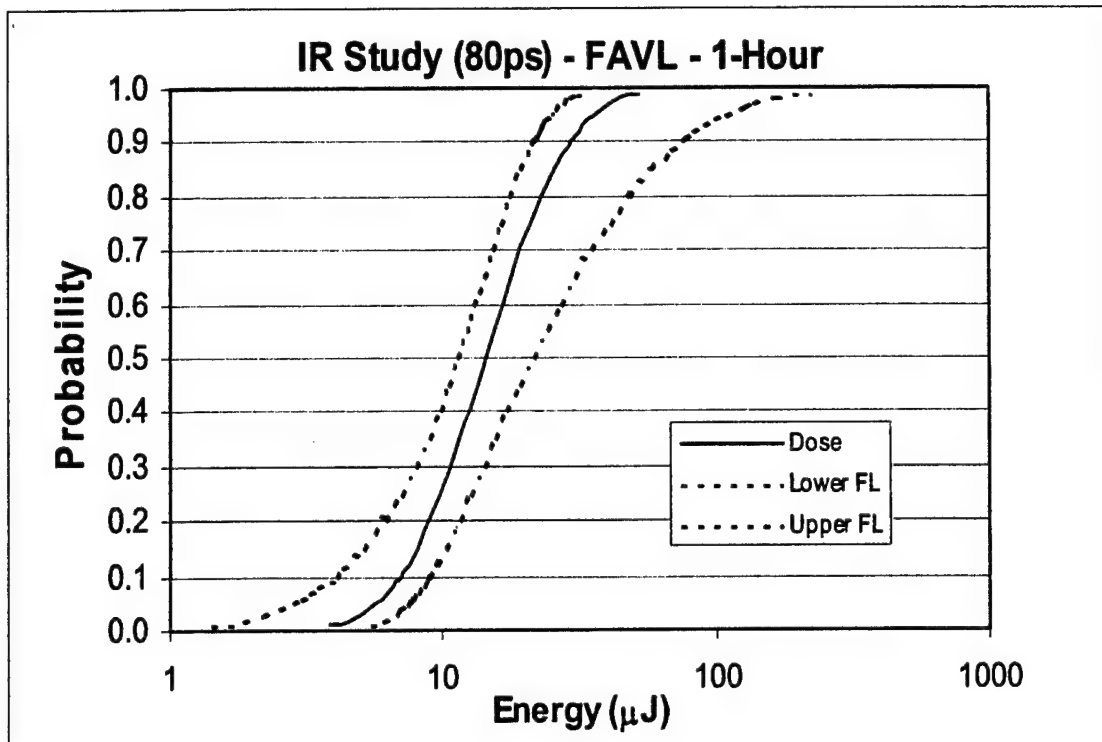
<u>Prob</u>	<u>Dose</u>	<u>LFL</u>	<u>UFL</u>	<u>Prob</u>	<u>Dose</u>	<u>LFL</u>	<u>UFL</u>
0.01	3.87	1.40	5.45	0.55	15.3	12.1	23.8
0.02	4.51	1.85	6.15	0.60	16.4	12.9	26.9
0.03	4.97	2.21	6.65	0.65	17.7	13.9	30.5
0.04	5.35	2.53	7.07	0.70	19.1	14.9	35.0
0.05	5.67	2.82	7.43	0.75	20.8	16.0	40.6
0.06	5.97	3.08	7.75	0.80	22.8	17.3	48.1
0.07	6.24	3.33	8.05	0.85	25.5	18.9	58.7
0.08	6.49	3.58	8.34	0.90	29.2	21.1	75.5
0.09	6.73	3.81	8.61	0.91	30.2	21.7	80.3
0.10	6.95	4.04	8.87	0.92	31.3	22.3	85.9
0.15	7.98	5.09	10.1	0.93	32.6	23.0	92.4
0.20	8.90	6.07	11.3	0.94	34.0	23.8	100.
0.25	9.77	7.00	12.6	0.95	35.8	24.8	110.
0.30	10.6	7.89	13.9	0.96	38.0	25.9	123.
0.35	11.5	8.75	15.4	0.97	40.8	27.4	141.
0.40	12.4	9.59	17.1	0.98	45.0	29.6	169.
0.45	13.3	10.4	19.1	0.99	52.4	33.2	226.
0.50	14.3	11.2	21.3				

<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>
0.450	1	0	2.60	1	0	8.80	1	0
0.540	1	0	2.63	1	0	9.00	1	0
0.600	2	0	2.69	1	0	9.10	1	0
0.720	1	0	2.70	1	0	9.30	1	0
0.770	1	0	2.77	1	0	9.40	1	0

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.830	1	0	2.87	1	0	9.49	1	1
0.900	1	0	3.15	1	0	9.85	1	1
1.00	1	0	3.34	1	0	10.2	1	0
1.06	1	0	3.44	1	0	10.3	1	0
1.10	2	0	3.50	1	0	11.0	1	0
1.13	2	0	3.53	1	0	11.2	1	0
1.15	1	0	3.90	1	0	11.6	2	0
1.20	2	0	3.94	1	0	11.7	1	0
1.27	1	0	4.00	1	1	12.2	1	0
1.30	1	0	5.00	1	0	14.9	1	1
1.36	1	0	5.21	1	0	17.4	1	1
1.38	1	0	5.24	1	0	18.2	1	1
1.43	1	0	5.74	1	0	19.0	1	0
1.53	1	0	5.85	1	0	21.0	1	1
1.56	1	0	6.04	1	0	22.6	1	1
1.84	1	0	6.19	1	0	25.7	1	1
1.88	1	0	6.23	1	0	27.0	1	1
1.90	1	0	6.30	1	0	32.6	1	1
1.95	1	0	6.52	1	0	36.8	1	1
2.05	1	0	6.90	1	1	37.0	1	1
2.12	1	0	7.13	1	0	38.0	1	1
2.30	1	0	7.14	1	0	40.0	1	1
2.34	1	0	7.17	1	0	40.3	1	1
2.42	1	0	7.53	1	0	51.0	1	1
2.49	1	0	7.80	1	0	53.6	1	1
2.50	1	0	7.87	1	0			
2.53	1	0	8.25	2	0			

**Totals**

**100 19**





**IR Study (80ps) - FAVL - 24-Hour**  
 963 OD, 987 OS, A35 OD, A47 OS, A13 OD

ONES =17    ZEROES = 83    TOTAL = 100

Percent confidence = 0.95

ED50 = 14.7    Upper FL = 20.6    Lower FL = 12.0

Intercept = -7.07    Slope = 6.05

Pearson's Chi-Sq = 58.4610    Probability of Chi-Sq = 0.9975

h = 1.00    g = 0.24    t = 1.96

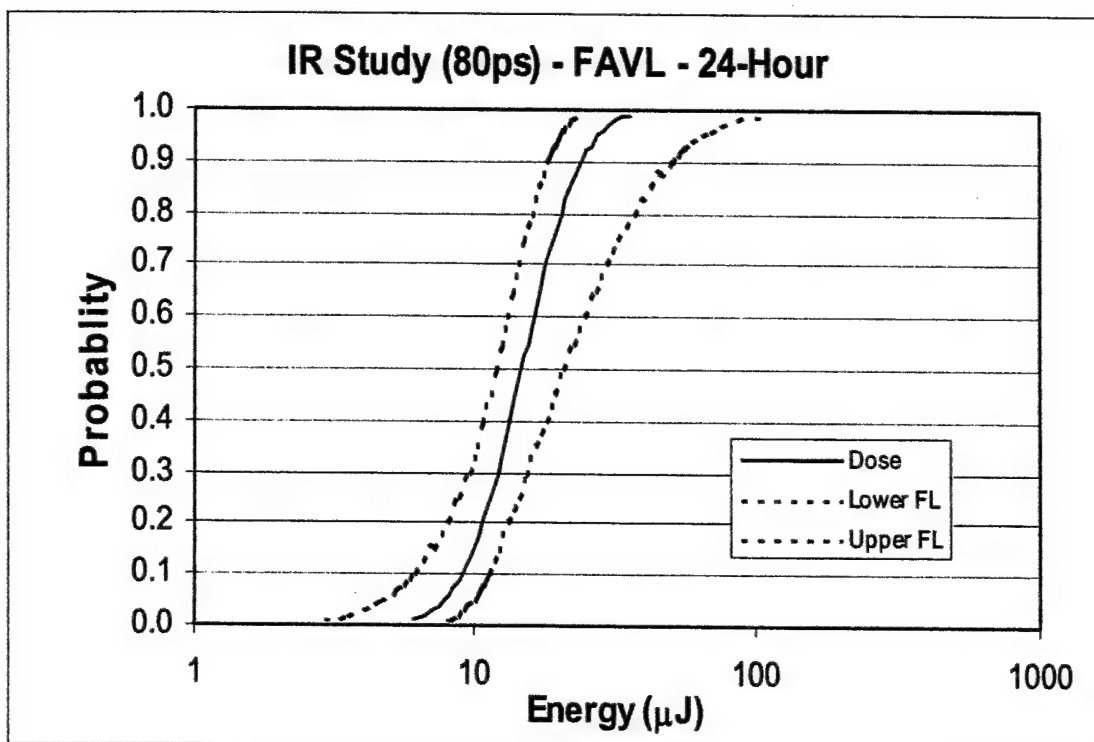
Log XBAR = 1.08    Log YBAR = 4.47

SYX = 74.268    SXY = 2.614    SXX = 0.432    S0 = 13.200

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	6.08	2.95	8.08	0.55	15.5	12.6	22.3
0.02	6.74	3.59	8.74	0.60	16.2	13.2	24.3
0.03	7.20	4.06	9.20	0.65	17.1	13.8	26.5
0.04	7.57	4.44	9.57	0.70	18.0	14.4	29.1
0.05	7.88	4.78	9.89	0.75	19.1	15.1	32.3
0.06	8.15	5.09	10.2	0.80	20.3	15.9	36.4
0.07	8.40	5.37	10.4	0.85	21.9	16.8	41.8
0.08	8.63	5.63	10.7	0.90	24.0	18.0	49.8
0.09	8.85	5.88	10.9	0.91	24.6	18.3	52.0
0.10	9.05	6.11	11.1	0.92	25.2	18.7	54.5
0.15	9.93	7.15	12.2	0.93	25.9	19.0	57.4
0.20	10.7	8.04	13.2	0.94	26.6	19.5	60.8
0.25	11.4	8.83	14.2	0.95	27.6	20.0	64.9
0.30	12.1	9.54	15.3	0.96	28.7	20.5	70.1
0.35	12.7	10.2	16.5	0.97	30.2	21.3	77.1
0.40	13.4	10.8	17.7	0.98	32.2	22.3	87.6
0.45	14.1	11.4	19.1	0.99	35.7	24.0	107.
0.50	14.7	12.0	20.6				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.450	1	0	2.60	1	0	8.80	1	0
0.540	1	0	2.63	1	0	9.00	1	0
0.600	2	0	2.69	1	0	9.10	1	0
0.720	1	0	2.70	1	0	9.30	1	0
0.770	1	0	2.77	1	0	9.40	1	0

<b>Dose</b>	<b>Tries</b>	<b>Hits</b>	<b>Dose</b>	<b>Tries</b>	<b>Hits</b>	<b>Dose</b>	<b>Tries</b>	<b>Hits</b>
0.830	1	0	2.87	1	0	9.49	1	1
0.900	1	0	3.15	1	0	9.85	1	0
1.00	1	0	3.34	1	0	10.2	1	0
1.06	1	0	3.44	1	0	10.3	1	0
1.10	2	0	3.50	1	0	11.0	1	0
1.13	2	0	3.53	1	0	11.2	1	0
1.15	1	0	3.90	1	0	11.6	2	0
1.20	2	0	3.94	1	0	11.7	1	0
1.27	1	0	4.00	1	0	12.2	1	0
1.30	1	0	5.00	1	0	14.9	1	1
1.36	1	0	5.21	1	0	17.4	1	1
1.38	1	0	5.24	1	0	18.2	1	1
1.43	1	0	5.74	1	0	19.0	1	0
1.53	1	0	5.85	1	0	21.0	1	1
1.56	1	0	6.04	1	0	22.6	1	1
1.84	1	0	6.19	1	0	25.7	1	1
1.88	1	0	6.23	1	0	27.0	1	1
1.90	1	0	6.30	1	0	32.6	1	1
1.95	1	0	6.52	1	0	36.8	1	1
2.05	1	0	6.90	1	1	37.0	1	1
2.12	1	0	7.13	1	0	38.0	1	1
2.30	1	0	7.14	1	0	40.0	1	1
2.34	1	0	7.17	1	0	40.3	1	1
2.42	1	0	7.53	1	0	51.0	1	1
2.49	1	0	7.80	1	0	53.6	1	1
2.50	1	0	7.87	1	0			
2.53	1	0	8.25	2	0			
<b>Totals</b>							<b>100</b>	<b>17</b>



**IR Study (20ps) - MVL - 1 Hour**

963 OS, A47 OD, A35 OS

ONES = 28

ZEROES = 44

TOTAL = 72

Percent confidence = 0.95

ED50 = 5.58 Upper FL = 6.84 Lower FL = 4.61

Intercept = -4.23 Slope = 5.66

Pearson's Chi-Sq = 24.8595 Probability of Chi-Sq = 0.9954

h = 1.00 g = 0.20 t = 1.96

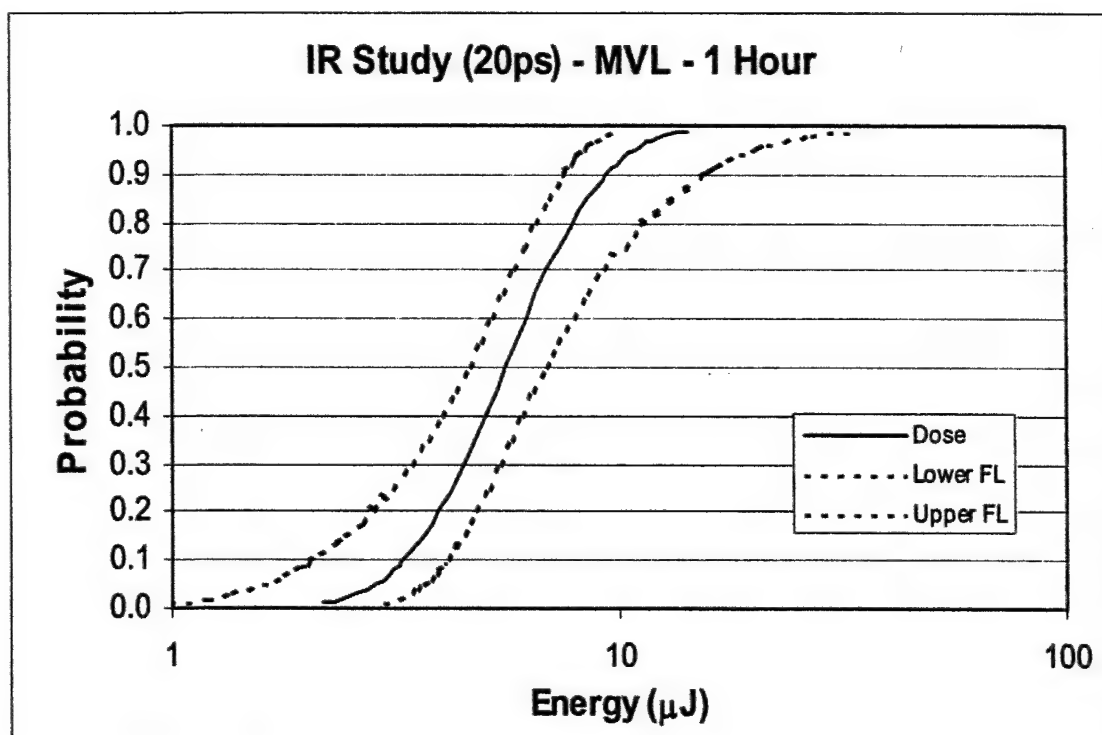
Log XBAR = 0.736 Log YBAR = 4.94

SYY = 43.849 SXY = 3.355 SXX = 0.593 S0 = 20.589

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	2.17	0.983	2.99	0.55	5.87	4.89	7.32
0.02	2.42	1.20	3.24	0.60	6.19	5.18	7.88
0.03	2.60	1.36	3.41	0.65	6.53	5.48	8.53
0.04	2.74	1.49	3.55	0.70	6.91	5.78	9.31
0.05	2.86	1.60	3.67	0.75	7.34	6.11	10.3
0.06	2.96	1.71	3.77	0.80	7.86	6.48	11.5
0.07	3.06	1.81	3.87	0.85	8.51	6.92	13.1
0.08	3.15	1.90	3.95	0.90	9.40	7.49	15.5
0.09	3.23	1.99	4.04	0.91	9.63	7.63	16.2
0.10	3.31	2.07	4.11	0.92	9.88	7.79	17.0
0.15	3.66	2.46	4.46	0.93	10.2	7.96	17.8
0.20	3.96	2.80	4.77	0.94	10.5	8.16	18.9
0.25	4.24	3.12	5.07	0.95	10.9	8.39	20.1
0.30	4.51	3.44	5.37	0.96	11.4	8.66	21.7
0.35	4.77	3.74	5.69	0.97	12.0	9.01	23.8
0.40	5.03	4.03	6.04	0.98	12.9	9.48	27.0
0.45	5.30	4.32	6.41	0.99	14.4	10.3	32.9
0.50	5.58	4.61	6.84				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.500	2	0	3.30	1	0	7.00	2	2
0.600	1	0	3.40	2	1	7.90	1	1
0.700	3	0	3.80	2	1	8.10	2	1
0.800	2	0	3.90	1	0	9.00	1	1
1.00	1	0	4.00	1	0	9.30	1	1

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
1.10	1	0	4.10	2	2	9.70	3	3
1.40	1	0	4.20	1	0	10.1	1	1
1.50	2	0	4.60	1	0	10.6	1	1
1.60	2	0	4.70	1	0	10.9	1	1
1.80	2	0	5.00	2	0	11.8	2	2
1.90	1	0	5.30	2	0	12.6	1	1
2.20	1	0	5.40	3	2	15.0	1	1
2.40	3	0	6.30	2	1	20.0	1	1
2.80	1	0	6.40	1	0	25.0	1	1
3.10	3	0	6.70	1	0	30.5	1	1
3.20	1	0	6.80	1	1	42.8	1	1
<b>Totals</b>							<b>72</b>	<b>28</b>



**IR Study (20ps) - MVL - 24 Hour**

963 OS, A47 OD, A35 OS

ONES = 34

ZEROES = 38

TOTAL = 72

Percent confidence = 0.95

ED50 = 4.63 Upper FL = 5.51 Lower FL = 3.84

Intercept = -4.43 Slope = 6.66

Pearson's Chi-Sq = 27.3373 Probability of Chi-Sq = 0.9869

h = 1.00 g = 0.22 t = 1.96

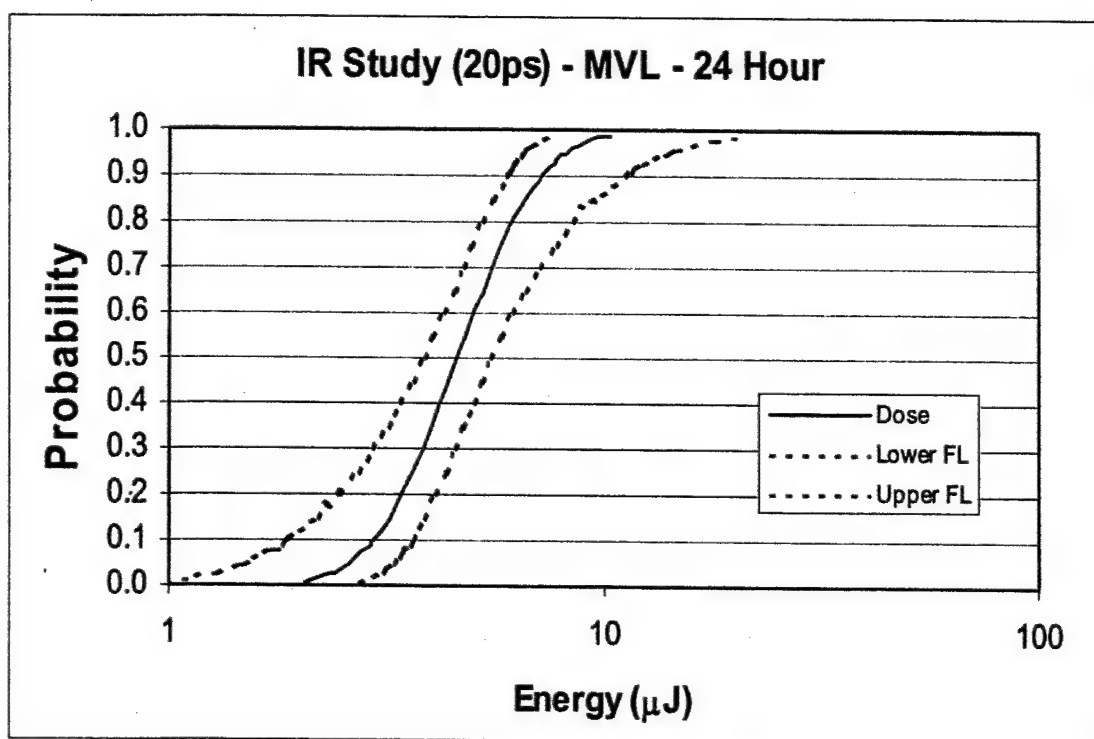
Log XBAR = 0.673 Log YBAR = 5.05

SYY = 45.041 SXY = 2.656 SXX = 0.399 S0 = 18.139

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	2.07	0.980	2.78	0.55	4.83	4.06	5.83
0.02	2.27	1.16	2.97	0.60	5.05	4.28	6.19
0.03	2.42	1.30	3.10	0.65	5.28	4.50	6.61
0.04	2.53	1.41	3.21	0.70	5.54	4.73	7.12
0.05	2.62	1.51	3.30	0.75	5.84	4.97	7.73
0.06	2.70	1.59	3.37	0.80	6.19	5.24	8.50
0.07	2.78	1.67	3.45	0.85	6.62	5.55	9.54
0.08	2.85	1.75	3.51	0.90	7.20	5.94	11.1
0.09	2.91	1.82	3.57	0.91	7.35	6.04	11.5
0.10	2.97	1.88	3.63	0.92	7.52	6.14	11.9
0.15	3.23	2.19	3.88	0.93	7.70	6.26	12.4
0.20	3.46	2.46	4.10	0.94	7.91	6.39	13.1
0.25	3.66	2.71	4.32	0.95	8.17	6.55	13.8
0.30	3.86	2.95	4.53	0.96	8.47	6.73	14.8
0.35	4.05	3.18	4.75	0.97	8.86	6.96	16.0
0.40	4.24	3.40	4.98	0.98	9.40	7.27	17.9
0.45	4.43	3.63	5.23	0.99	10.3	7.78	21.2
0.50	4.63	3.84	5.51				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.500	2	0	3.30	1	0	7.00	2	2
0.600	1	0	3.40	2	0	7.90	1	1
0.700	3	0	3.80	2	1	8.10	2	2
0.800	2	0	3.90	1	0	9.00	1	1
1.00	1	0	4.00	1	1	9.30	1	1

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
1.10	1	0	4.10	2	2	9.70	3	3
1.40	1	0	4.20	1	1	10.1	1	1
1.50	2	0	4.60	1	0	10.6	1	1
1.60	2	0	4.70	1	0	10.9	1	1
1.80	2	0	5.00	2	2	11.8	2	2
1.90	1	0	5.30	2	1	12.6	1	1
2.20	1	0	5.40	3	3	15.0	1	1
2.40	3	0	6.30	2	1	20.0	1	1
2.80	1	0	6.40	1	0	25.0	1	1
3.10	3	0	6.70	1	0	30.5	1	1
3.20	1	0	6.80	1	1	42.8	1	1
Totals							72	34





**IR Study (20ps) - FAVL - 1 Hour**  
963 OS, A47 OD, A35 OS

ONES = 14                      ZEROES = 58                      TOTAL = 72

Percent confidence = 0.95

ED50 = 15.9    Upper FL = 296.                      Lower FL = 8.56

Intercept = -2.11                      Slope = 1.76

Pearson's Chi-Sq = 61.2213    Probability of Chi-Sq = 0.0659

h = 1.33                      g = 0.55                      t = 2.01

Log XBAR = 0.787    Log YBAR = 4.27

SY Y = 71.078 SXY = 5.601    SXX = 3.182    S0 = 28.758

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.757	0.00288	1.28	0.55	18.7	12.6	413.
0.02	1.08	0.0103	1.72	0.60	22.1	14.7	743.
0.03	1.36	0.0231	2.09	0.65	26.3	17.1	1.37e+003
0.04	1.61	0.0421	2.43	0.70	31.5	20.1	2.61e+003
0.05	1.85	0.0686	2.75	0.75	38.4	23.7	5.25e+003
0.06	2.08	0.104	3.07	0.80	47.8	28.5	1.15e+004
0.07	2.30	0.148	3.38	0.85	61.6	35.2	2.86e+004
0.08	2.53	0.204	3.70	0.90	84.9	45.8	9.07e+004
0.09	2.75	0.272	4.02	0.91	91.8	48.8	1.20e+005
0.10	2.97	0.353	4.36	0.92	99.8	52.3	1.62e+005
0.15	4.09	0.999	6.35	0.93	110.	56.4	2.26e+005
0.20	5.28	2.07	9.44	0.94	121.	61.3	3.28e+005
0.25	6.57	3.43	15.0	0.95	137.	67.5	5.02e+005
0.30	8.00	4.86	25.2	0.96	157.	75.5	8.28e+005
0.35	9.59	6.27	43.5	0.97	186.	86.7	1.53e+006
0.40	11.4	7.70	76.0	0.98	233.	104.	3.46e+006
0.45	13.5	9.21	133.	0.99	333.	139.	1.25e+007
0.50	15.9	10.8	233.				

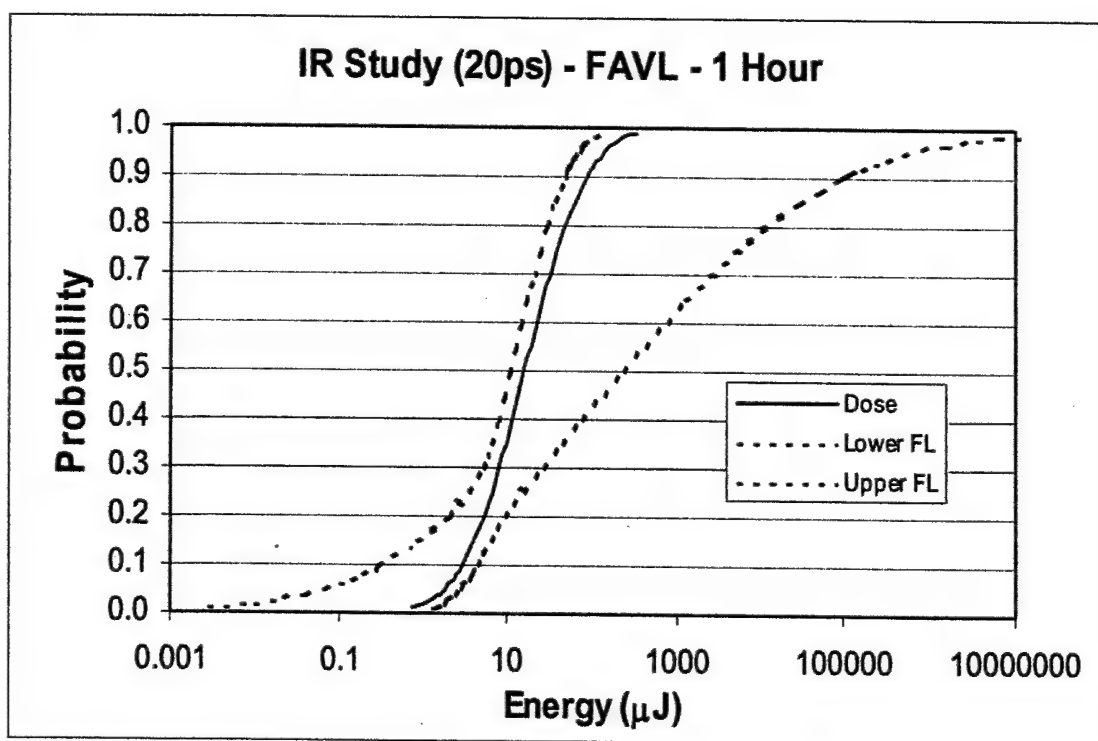
Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.500	2	0	3.30	1	0	7.00	2	2
0.600	1	0	3.40	2	1	7.90	1	0
0.700	3	1	3.80	2	0	8.10	2	0
0.800	2	0	3.90	1	0	9.00	1	0
1.00	1	0	4.00	1	0	9.30	1	0

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
1.10	1	0	4.10	2	0	9.70	3	1
1.40	1	0	4.20	1	0	10.1	1	0
1.50	2	0	4.60	1	0	10.6	1	0
1.60	2	0	4.70	1	0	10.9	1	0
1.80	2	0	5.00	2	1	11.8	2	1
1.90	1	0	5.30	2	0	12.6	1	1
2.20	1	0	5.40	3	1	15.0	1	1
2.40	3	0	6.30	2	0	20.0	1	1
2.80	1	0	6.40	1	0	25.0	1	1
3.10	3	0	6.70	1	0	30.5	1	1
3.20	1	0	6.80	1	0	42.8	1	1

Totals

72

14



**IR Study (20ps) - FAVL - 24 Hour**  
963 OS, A47 OD, A35 OS

ONES = 7                      ZEROES = 65                      TOTAL = 72

Percent confidence = 0.95

ED50 = 51.4    Upper FL = 1.64e-007                      Lower FL = 14.5

Intercept = -2.28              Slope = 1.33

Pearson's Chi-Sq = 66.4613    Probability of Chi-Sq = 0.0258

h = 1.44              g = 1.24              t = 2.01

Log XBAR = 0.822                      Log YBAR = 3.82

SYX = 71.164    SXY = 3.533    SXX = 2.654    S0 = 20.986

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.920	3.23e+007	13.9	0.55	63.9	2.97	1.35e-007
0.02	1.47	7.48e+005	12.7	0.60	79.7	2.82	2.35e-008
0.03	1.99	6.71e+004	12.3	0.65	100.	2.67	3.85e-009
0.04	2.49	1.07e+004	12.3	0.70	127.	2.51	5.74e-010
0.05	2.99	2.31e+003	12.7	0.75	165.	2.34	7.36e-011
0.06	3.49	597.	13.8	0.80	221.	2.17	7.49e-012
0.07	4.01	162.	16.7	0.85	309.	1.98	5.23e-013
0.08	4.53	-1.#J	-1.#J	0.90	472.	1.77	1.84e-014
0.09	5.06	-1.#J	-1.#J	0.91	523.	1.72	8.20e-015
0.10	5.61	-1.#J	-1.#J	0.92	585.	1.66	3.41e-015
0.15	8.57	-1.#J	-1.#J	0.93	661.	1.61	1.30e-015
0.20	12.0	3.04	0.114	0.94	757.	1.55	4.42e-016
0.25	16.0	3.52	0.00929	0.95	885.	1.48	1.29e-016
0.30	20.8	3.58	0.00110	0.96	1.06e+003	1.41	3.05e-017
0.35	26.4	3.51	0.000157	0.97	1.33e+003	1.32	5.17e-018
0.40	33.2	3.40	2.51e-005	0.98	1.80e+003	1.21	4.88e-019
0.45	41.4	3.26	4.30e-006	0.99	2.88e+003	1.06	1.19e-020
0.50	51.4	3.12	7.62e-007				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.500	2	0	3.30	1	0	7.00	2	0
0.600	1	0	3.40	2	0	7.90	1	0
0.700	3	1	3.80	2	0	8.10	2	0
0.800	2	0	3.90	1	0	9.00	1	0
1.00	1	0	4.00	1	0	9.30	1	0

<b>Dose</b>	<b>Tries</b>	<b>Hits</b>	<b>Dose</b>	<b>Tries</b>	<b>Hits</b>	<b>Dose</b>	<b>Tries</b>	<b>Hits</b>
1.10	1	0	4.10	2	0	9.70	3	1
1.40	1	0	4.20	1	0	10.1	1	0
1.50	2	0	4.60	1	0	10.6	1	0
1.60	2	0	4.70	1	0	10.9	1	0
1.80	2	0	5.00	2	0	11.8	2	0
1.90	1	0	5.30	2	0	12.6	1	1
2.20	1	0	5.40	3	1	15.0	1	0
2.40	3	0	6.30	2	0	20.0	1	0
2.80	1	0	6.40	1	0	25.0	1	1
3.10	3	0	6.70	1	0	30.5	1	1
3.20	1	0	6.80	1	0	42.8	1	1
<b>Totals</b>							<b>72</b>	<b>7</b>

**IR Study (1ps) - MVL - 1 Hour**  
**C03 OD, C05 OS, C03 OS**

ONES = 23    ZEROES = 49    TOTAL = 72

Percent confidence = 0.95

ED50 = 3.80    Upper FL = 5.60    Lower FL = 2.99

Intercept = -1.93    Slope = 3.34

Pearson's Chi-Sq = 58.1886    Probability of Chi-Sq = 0.7701

h = 1.00    g = 0.26    t = 1.96

Log XBAR = 0.490    Log YBAR = 4.70

SYX = 72.835    SXY = 4.391    SXX = 1.316    S0 = 32.005

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.763	0.169	1.27	0.55	4.14	3.26	6.50
0.02	0.921	0.247	1.45	0.60	4.53	3.53	7.62
0.03	1.04	0.314	1.58	0.65	4.96	3.81	9.03
0.04	1.14	0.376	1.68	0.70	5.46	4.12	10.8
0.05	1.22	0.435	1.77	0.75	6.05	4.46	13.2
0.06	1.30	0.492	1.85	0.80	6.79	4.87	16.6
0.07	1.37	0.549	1.93	0.85	7.77	5.37	21.7
0.08	1.44	0.604	2.00	0.90	9.21	6.05	30.4
0.09	1.51	0.659	2.07	0.91	9.59	6.23	33.0
0.10	1.57	0.714	2.13	0.92	10.0	6.43	36.1
0.15	1.86	0.990	2.43	0.93	10.5	6.65	39.9
0.20	2.13	1.27	2.72	0.94	11.1	6.90	44.5
0.25	2.39	1.56	3.03	0.95	11.8	7.21	50.4
0.30	2.65	1.86	3.38	0.96	12.7	7.58	58.5
0.35	2.91	2.15	3.78	0.97	13.9	8.06	70.1
0.40	3.19	2.44	4.27	0.98	15.7	8.75	89.3
0.45	3.48	2.72	4.86	0.99	18.9	9.94	131.
0.50	3.80	2.99	5.60				

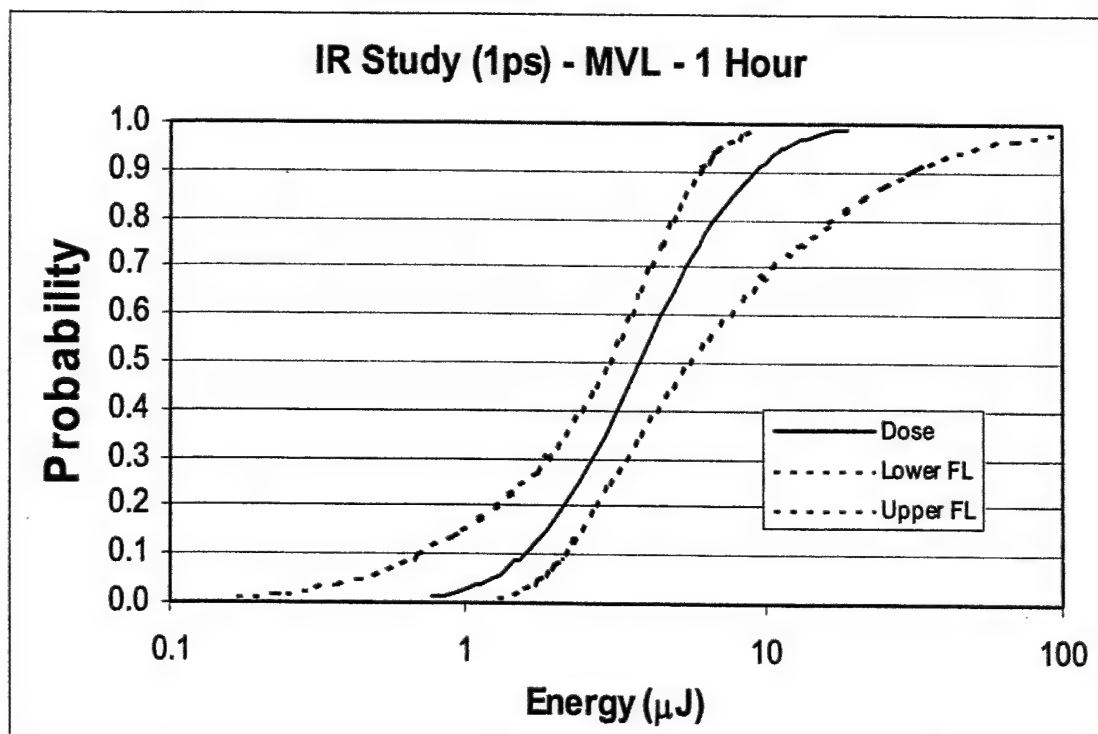
Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.170	1	0	1.74	1	0	3.53	1	1
0.300	1	0	1.79	1	0	3.54	1	1
0.390	1	0	1.86	1	0	3.58	1	0
0.550	1	0	1.92	1	0	3.59	1	0
0.580	1	0	2.00	1	1	3.61	1	0

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.610	1	0	2.07	1	0	3.66	1	0
0.710	1	0	2.09	2	0	3.87	1	0
0.750	1	0	2.14	1	0	4.08	1	0
0.810	1	0	2.26	1	0	4.14	1	1
0.830	1	0	2.32	1	0	4.17	1	0
0.880	1	0	2.49	2	2	4.30	2	2
1.00	1	0	2.52	1	1	4.70	1	1
1.19	1	0	2.53	1	1	4.72	1	0
1.27	1	0	2.80	1	0	4.80	1	1
1.32	1	0	3.13	1	0	5.10	1	0
1.44	1	0	3.20	1	0	5.20	1	0
1.49	1	0	3.25	1	1	5.59	1	0
1.52	1	0	3.28	1	1	5.70	1	1
1.57	1	0	3.29	1	1	5.90	1	1
1.62	1	0	3.30	1	0	6.50	1	1
1.69	1	0	3.31	1	1	6.70	1	1
1.71	1	0	3.44	1	0	6.80	1	1
1.72	1	1	3.50	1	0	7.10	1	1

Totals

72

23



**IR Study (1ps) - MVL - 24 Hour**  
**C03 OD, C05 OS, C03 OS**

ONES = 42    ZEROES = 30    TOTAL = 72

Percent confidence = 0.95

ED50 = 1.96    Upper FL = 2.52    Lower FL = 1.40

Intercept = -0.922    Slope = 3.15

Pearson's Chi-Sq = 69.6849    Probability of Chi-Sq = 0.3873

h = 1.00    g = 0.20    t = 1.96

Log XBAR = 0.371    Log YBAR = 5.25

SYX = 89.011    SXY = 6.132    SXX = 1.945    S0 = 33.368

<u>Prob</u>	<u>Dose</u>	<u>LFL</u>	<u>UFL</u>	<u>Prob</u>	<u>Dose</u>	<u>LFL</u>	<u>UFL</u>
0.01	0.358	0.0762	0.663	0.55	2.15	1.59	2.79
0.02	0.437	0.109	0.765	0.60	2.36	1.79	3.12
0.03	0.496	0.136	0.837	0.65	2.60	2.01	3.53
0.04	0.546	0.161	0.896	0.70	2.88	2.24	4.08
0.05	0.590	0.185	0.948	0.75	3.21	2.50	4.81
0.06	0.630	0.208	0.994	0.80	3.63	2.80	5.83
0.07	0.667	0.230	1.04	0.85	4.18	3.16	7.37
0.08	0.703	0.252	1.08	0.90	5.00	3.65	9.98
0.09	0.736	0.274	1.11	0.91	5.22	3.77	10.7
0.10	0.769	0.295	1.15	0.92	5.47	3.91	11.7
0.15	0.920	0.404	1.32	0.93	5.76	4.07	12.7
0.20	1.06	0.516	1.47	0.94	6.11	4.25	14.1
0.25	1.20	0.636	1.62	0.95	6.52	4.47	15.8
0.30	1.34	0.765	1.77	0.96	7.05	4.73	18.1
0.35	1.48	0.904	1.93	0.97	7.75	5.07	21.4
0.40	1.63	1.06	2.10	0.98	8.79	5.56	26.7
0.45	1.79	1.22	2.29	0.99	10.7	6.43	38.1
0.50	1.96	1.40	2.52				

<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>
0.170	1	0	1.74	1	0	3.53	1	1
0.300	1	0	1.79	1	0	3.54	1	1
0.390	1	0	1.86	1	0	3.58	1	0
0.550	1	0	1.92	1	0	3.59	1	1
0.580	1	0	2.00	1	1	3.61	1	1

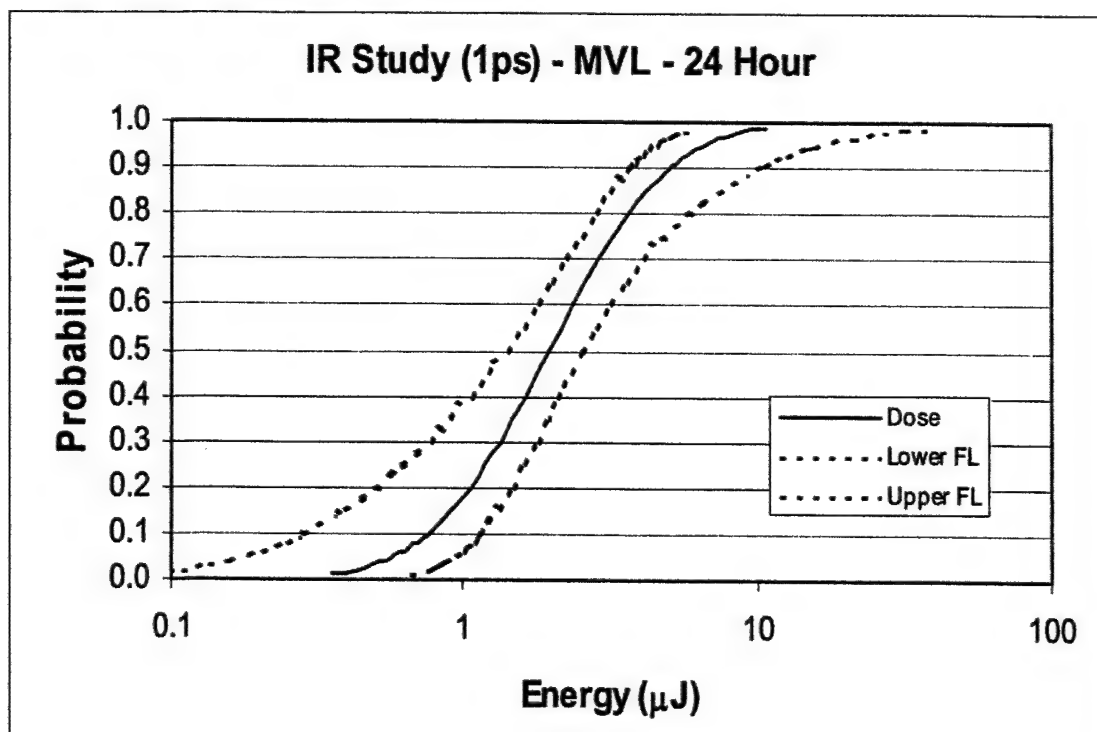


Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.610	1	0	2.07	1	1	3.66	1	1
0.710	1	0	2.09	2	1	3.87	1	1
0.750	1	0	2.14	1	1	4.08	1	1
0.810	1	0	2.26	1	1	4.14	1	1
0.830	1	0	2.32	1	1	4.17	1	1
0.880	1	0	2.49	2	2	4.30	2	2
1.00	1	0	2.52	1	1	4.70	1	1
1.19	1	0	2.53	1	1	4.72	1	0
1.27	1	0	2.80	1	0	4.80	1	1
1.32	1	0	3.13	1	1	5.10	1	1
1.44	1	1	3.20	1	0	5.20	1	0
1.49	1	1	3.25	1	1	5.59	1	0
1.52	1	0	3.28	1	1	5.70	1	1
1.57	1	0	3.29	1	1	5.90	1	1
1.62	1	1	3.30	1	1	6.50	1	1
1.69	1	0	3.31	1	1	6.70	1	1
1.71	1	1	3.44	1	0	6.80	1	1
1.72	1	1	3.50	1	1	7.10	1	1

Totals

72

42



**IR Study (1ps) - FAVL - 1 Hour**  
**C03 OD, C05 OS, C03 OS**

ONES = 6      ZEROES = 66      TOTAL = 72

Percent confidence = 0.95

ED50 = 6.79    Upper FL = 29.5      Lower FL = 5.23

Intercept = -4.36      Slope = 5.24

Pearson's Chi-Sq = 34.9398    Probability of Chi-Sq = 0.9996

h = 1.00      g = 0.59      t = 1.96

Log XBAR = 0.651    Log YBAR = 4.06

SYX = 41.420 SXY = 1.236    SXX = 0.236    S0 = 13.886

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	2.44	0.303	3.36	0.55	7.17	5.44	37.1
0.02	2.75	0.504	3.65	0.60	7.58	5.66	47.0
0.03	2.97	0.693	3.85	0.65	8.04	5.88	60.1
0.04	3.15	0.878	4.02	0.70	8.54	6.12	78.0
0.05	3.30	1.06	4.18	0.75	9.12	6.38	103.
0.06	3.43	1.24	4.33	0.80	9.82	6.68	142.
0.07	3.55	1.43	4.47	0.85	10.7	7.04	205.
0.08	3.66	1.61	4.62	0.90	11.9	7.52	325.
0.09	3.77	1.79	4.77	0.91	12.2	7.64	364.
0.10	3.87	1.97	4.92	0.92	12.6	7.76	411.
0.15	4.30	2.80	5.88	0.93	13.0	7.91	470.
0.20	4.69	3.45	7.26	0.94	13.4	8.07	546.
0.25	5.05	3.92	9.18	0.95	14.0	8.27	648.
0.30	5.39	4.26	11.7	0.96	14.6	8.50	792.
0.35	5.73	4.55	14.8	0.97	15.5	8.79	1.01e+003
0.40	6.07	4.79	18.6	0.98	16.7	9.19	1.41e+003
0.45	6.42	5.02	23.4	0.99	18.8	9.85	2.36e+003
0.50	6.79	5.23	29.5				

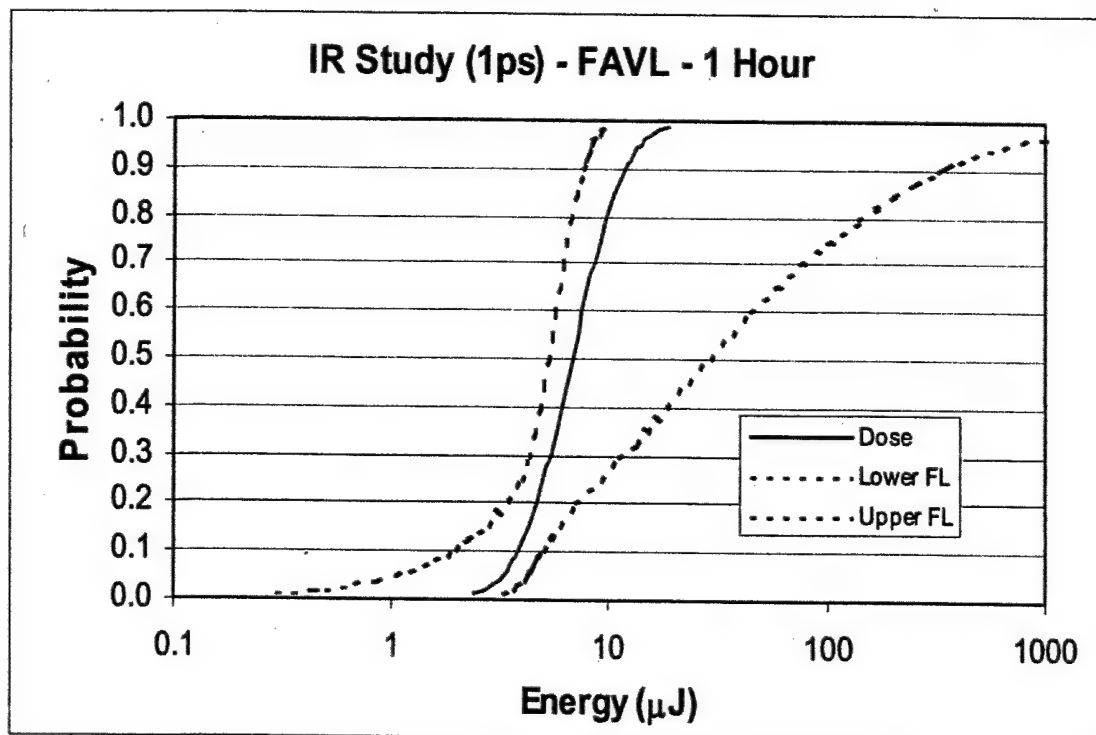
Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.170	1	0	1.74	1	0	3.53	1	0
0.300	1	0	1.79	1	0	3.54	1	0
0.390	1	0	1.86	1	0	3.58	1	0
0.550	1	0	1.92	1	0	3.59	1	0
0.580	1	0	2.00	1	0	3.61	1	0

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.610	1	0	2.07	1	0	3.66	1	0
0.710	1	0	2.09	2	0	3.87	1	0
0.750	1	0	2.14	1	0	4.08	1	0
0.810	1	0	2.26	1	0	4.14	1	0
0.830	1	0	2.32	1	0	4.17	1	0
0.880	1	0	2.49	2	0	4.30	2	1
1.00	1	0	2.52	1	0	4.70	1	0
1.19	1	0	2.53	1	0	4.72	1	0
1.27	1	0	2.80	1	0	4.80	1	0
1.32	1	0	3.13	1	0	5.10	1	0
1.44	1	0	3.20	1	0	5.20	1	1
1.49	1	0	3.25	1	1	5.59	1	0
1.52	1	0	3.28	1	0	5.70	1	1
1.57	1	0	3.29	1	0	5.90	1	0
1.62	1	0	3.30	1	0	6.50	1	1
1.69	1	0	3.31	1	0	6.70	1	0
1.71	1	0	3.44	1	0	6.80	1	1
1.72	1	0	3.50	1	0	7.10	1	0

Totals

72

6



**IR Study (1ps) - FAVL - 24 Hour**  
**C03 OD, C05 OS, C03 OS**

ONES = 9      ZEROES = 63      TOTAL = 72

Percent confidence = 0.95

ED50 = 5.15    Upper FL = 6.54      Lower FL = 4.52

Intercept = -7.12      Slope = 10.0

Pearson's Chi-Sq = 45.5543    Probability of Chi-Sq = 0.9793

h = 1.00      g = 0.33      t = 1.96

Log XBAR = 0.664    Log YBAR = 4.52

SYX = 57.222    SXY = 1.167    SXX = 0.117    S0 = 11.977

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	3.01	1.64	3.64	0.55	5.30	4.65	6.92
0.02	3.21	1.90	3.81	0.60	5.46	4.78	7.35
0.03	3.34	2.07	3.92	0.65	5.63	4.91	7.83
0.04	3.44	2.22	4.01	0.70	5.81	5.05	8.39
0.05	3.53	2.34	4.09	0.75	6.01	5.19	9.04
0.06	3.60	2.45	4.15	0.80	6.25	5.35	9.84
0.07	3.67	2.54	4.22	0.85	6.54	5.53	10.9
0.08	3.73	2.63	4.27	0.90	6.92	5.76	12.4
0.09	3.78	2.72	4.33	0.91	7.01	5.82	12.7
0.10	3.83	2.80	4.38	0.92	7.12	5.88	13.2
0.15	4.06	3.14	4.62	0.93	7.23	5.95	13.7
0.20	4.24	3.42	4.85	0.94	7.37	6.02	14.3
0.25	4.41	3.66	5.08	0.95	7.52	6.11	15.0
0.30	4.56	3.87	5.33	0.96	7.70	6.21	15.8
0.35	4.71	4.06	5.59	0.97	7.94	6.34	16.9
0.40	4.86	4.22	5.88	0.98	8.26	6.52	18.6
0.45	5.00	4.38	6.19	0.99	8.80	6.80	21.5
0.50	5.15	4.52	6.54				

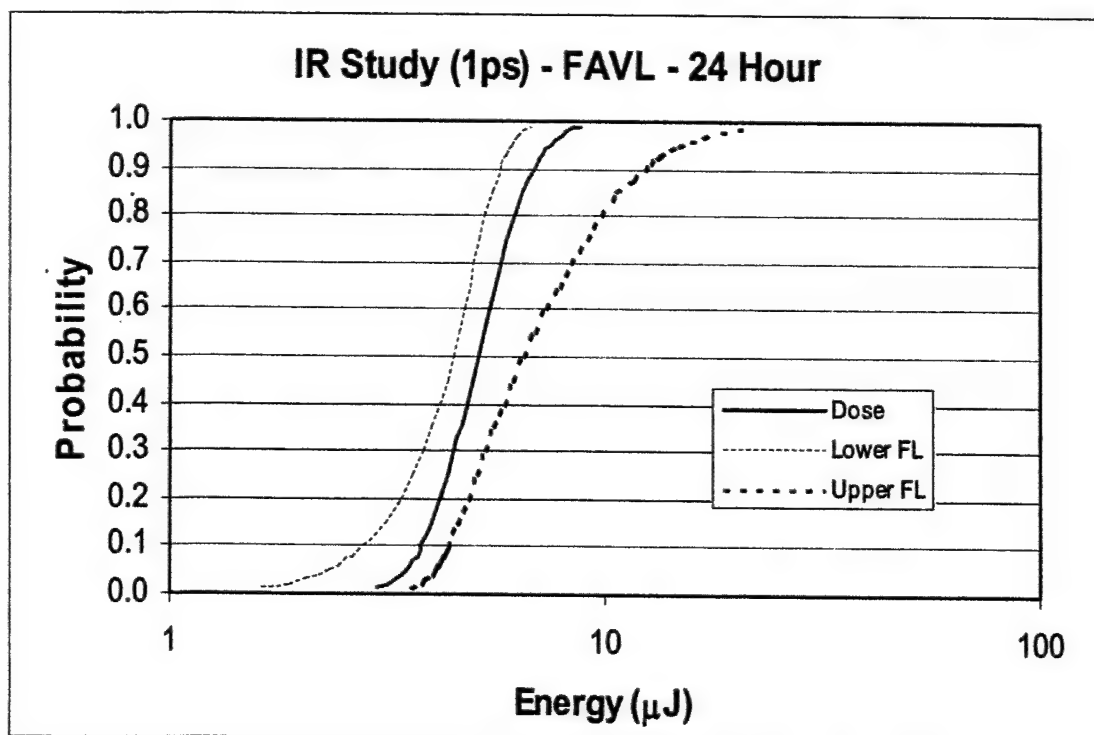
Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.170	1	0	1.74	1	0	3.53	1	0
0.300	1	0	1.79	1	0	3.54	1	0
0.390	1	0	1.86	1	0	3.58	1	0
0.550	1	0	1.92	1	0	3.59	1	0
0.580	1	0	2.00	1	0	3.61	1	0

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.610	1	0	2.07	1	0	3.66	1	0
0.710	1	0	2.09	2	0	3.87	1	0
0.750	1	0	2.14	1	0	4.08	1	0
0.810	1	0	2.26	1	0	4.14	1	0
0.830	1	0	2.32	1	0	4.17	1	0
0.880	1	0	2.49	2	0	4.30	2	1
1.00	1	0	2.52	1	0	4.70	1	0
1.19	1	0	2.53	1	0	4.72	1	0
1.27	1	0	2.80	1	0	4.80	1	0
1.32	1	0	3.13	1	0	5.10	1	0
1.44	1	0	3.20	1	0	5.20	1	1
1.49	1	0	3.25	1	0	5.59	1	0
1.52	1	0	3.28	1	0	5.70	1	1
1.57	1	0	3.29	1	0	5.90	1	1
1.62	1	0	3.30	1	1	6.50	1	1
1.69	1	0	3.31	1	0	6.70	1	1
1.71	1	0	3.44	1	0	6.80	1	1
1.72	1	0	3.50	1	0	7.10	1	1

Totals

72

9



**IR Study (150fs) - MVL - 1 Hour**  
A11 OS, A14 OS, C05 OD, C15 OS

ONES = 38    ZEROES = 43    TOTAL = 81

Percent confidence = 0.95

ED50 = 1.78    Upper FL = 2.67    Lower FL = 1.23

Intercept = -0.526    Slope = 2.11

Pearson's Chi-Sq = 68.5424    Probability of Chi-Sq = 0.5937

h = 1.00    g = 0.17    t = 1.96

Log XBAR = 0.201    Log YBAR = 4.90

SY Y = 91.547 SXY = 10.904 SXX = 5.169    S0 = 37.331

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.140	0.0246	0.301	0.55	2.04	1.43	3.20
0.02	0.189	0.0404	0.375	0.60	2.34	1.65	3.88
0.03	0.228	0.0553	0.431	0.65	2.70	1.89	4.78
0.04	0.263	0.0699	0.480	0.70	3.15	2.17	6.01
0.05	0.295	0.0846	0.523	0.75	3.71	2.50	7.73
0.06	0.325	0.0994	0.564	0.80	4.45	2.90	10.3
0.07	0.355	0.114	0.602	0.85	5.50	3.44	14.5
0.08	0.383	0.130	0.639	0.90	7.19	4.23	22.4
0.09	0.411	0.146	0.674	0.91	7.67	4.44	24.9
0.10	0.438	0.162	0.709	0.92	8.23	4.68	28.0
0.15	0.573	0.248	0.877	0.93	8.89	4.97	31.7
0.20	0.709	0.347	1.05	0.94	9.69	5.30	36.6
0.25	0.850	0.459	1.23	0.95	10.7	5.70	43.0
0.30	1.00	0.585	1.43	0.96	12.0	6.21	52.1
0.35	1.17	0.725	1.66	0.97	13.8	6.90	66.0
0.40	1.35	0.880	1.93	0.98	16.7	7.94	90.3
0.45	1.55	1.05	2.26	0.99	22.5	9.87	148.
0.50	1.78	1.23	2.67				

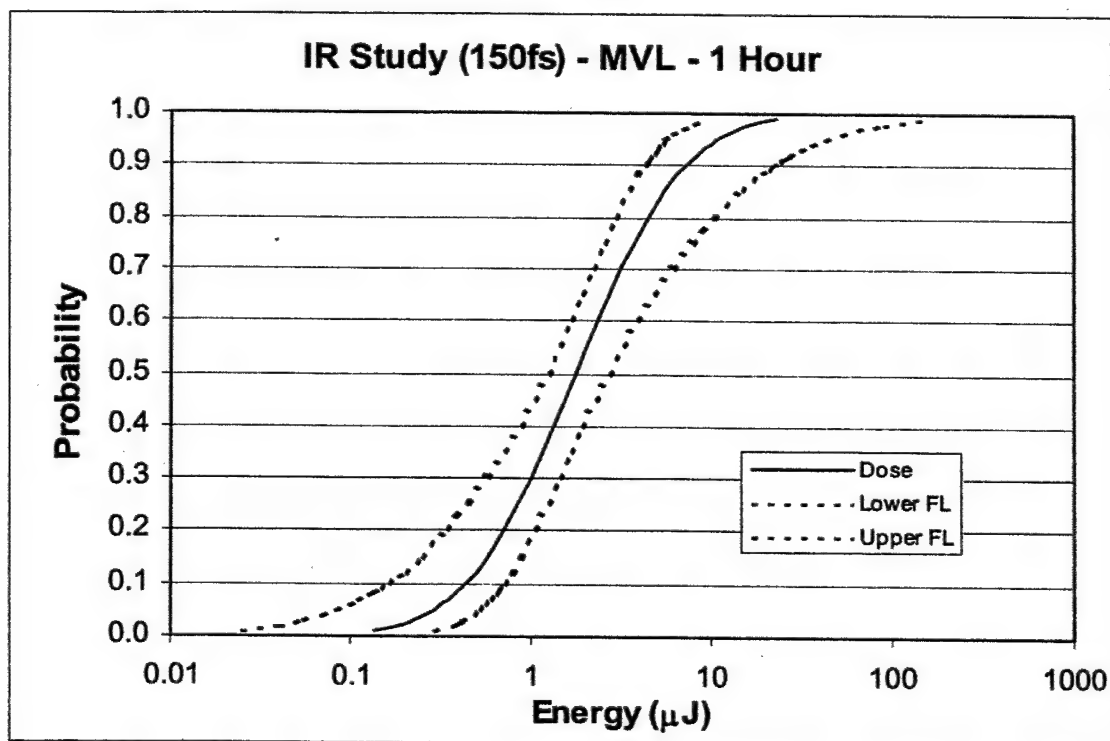
Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.00200		1	0	1.05	1	1	2.55	1
0.120	1	0	1.16	1	0	2.60	1	0
0.180	1	0	1.19	1	0	2.61	1	0
0.210	1	0	1.22	1	1	2.96	1	0
0.350	1	0	1.25	1	0	3.00	1	0

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.380	2	0	1.28	1	0	3.73	1	1
0.400	2	0	1.30	2	1	3.90	1	1
0.420	1	0	1.38	1	0	4.10	1	0
0.500	1	0	1.40	1	1	4.29	1	1
0.510	1	1	1.44	1	0	4.76	1	1
0.520	2	0	1.50	1	1	6.00	1	1
0.530	2	0	1.51	1	1	6.83	1	1
0.580	1	0	1.61	1	0	7.10	1	1
0.640	1	0	1.64	1	0	7.13	1	1
0.690	1	0	1.67	1	0	8.35	1	1
0.700	1	0	1.81	1	1	8.40	1	0
0.730	1	1	1.85	1	1	8.70	1	1
0.740	1	0	1.90	1	0	10.9	1	1
0.770	1	0	1.97	1	1	11.4	1	1
0.780	1	0	2.02	1	1	11.7	1	1
0.810	1	0	2.11	1	1	12.5	2	2
0.950	2	1	2.12	1	0	13.4	1	1
0.970	1	0	2.17	1	1	13.7	1	1
1.02	1	1	2.48	1	1	13.9	1	1
1.03	1	1	2.51	1	1			

Totals

81

38





**IR Study (150fs) - MVL - 24 Hour**  
A11 OS, A14 OS, C05 OD, C15 OS

ONES = 52    ZEROES = 29    TOTAL = 81

Percent confidence = 0.95

ED50 = 0.969 Upper FL = 1.20    Lower FL = 0.754

Intercept = 0.0598    Slope = 4.42

Pearson's Chi-Sq = 48.5680    Probability of Chi-Sq = 0.9846

h = 1.00    g = 0.18    t = 1.96

Log XBAR = 0.0199    Log YBAR = 5.15

SYX = 70.159 SXY = 4.888    SXX = 1.107    S0 = 23.812

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.288	0.108	0.439	0.55	1.03	0.819	1.30
0.02	0.332	0.138	0.488	0.60	1.11	0.887	1.41
0.03	0.364	0.160	0.522	0.65	1.18	0.958	1.55
0.04	0.389	0.180	0.549	0.70	1.27	1.03	1.71
0.05	0.411	0.197	0.572	0.75	1.38	1.12	1.92
0.06	0.431	0.213	0.593	0.80	1.50	1.21	2.19
0.07	0.449	0.229	0.612	0.85	1.66	1.32	2.56
0.08	0.466	0.243	0.629	0.90	1.89	1.47	3.15
0.09	0.482	0.257	0.645	0.91	1.95	1.50	3.31
0.10	0.497	0.271	0.661	0.92	2.02	1.55	3.49
0.15	0.565	0.334	0.731	0.93	2.09	1.59	3.71
0.20	0.625	0.393	0.794	0.94	2.18	1.64	3.97
0.25	0.682	0.452	0.855	0.95	2.28	1.70	4.30
0.30	0.737	0.510	0.916	0.96	2.41	1.78	4.71
0.35	0.793	0.569	0.979	0.97	2.58	1.87	5.27
0.40	0.849	0.629	1.05	0.98	2.83	2.00	6.14
0.45	0.908	0.691	1.12	0.99	3.26	2.23	7.80
0.50	0.969	0.754	1.20				

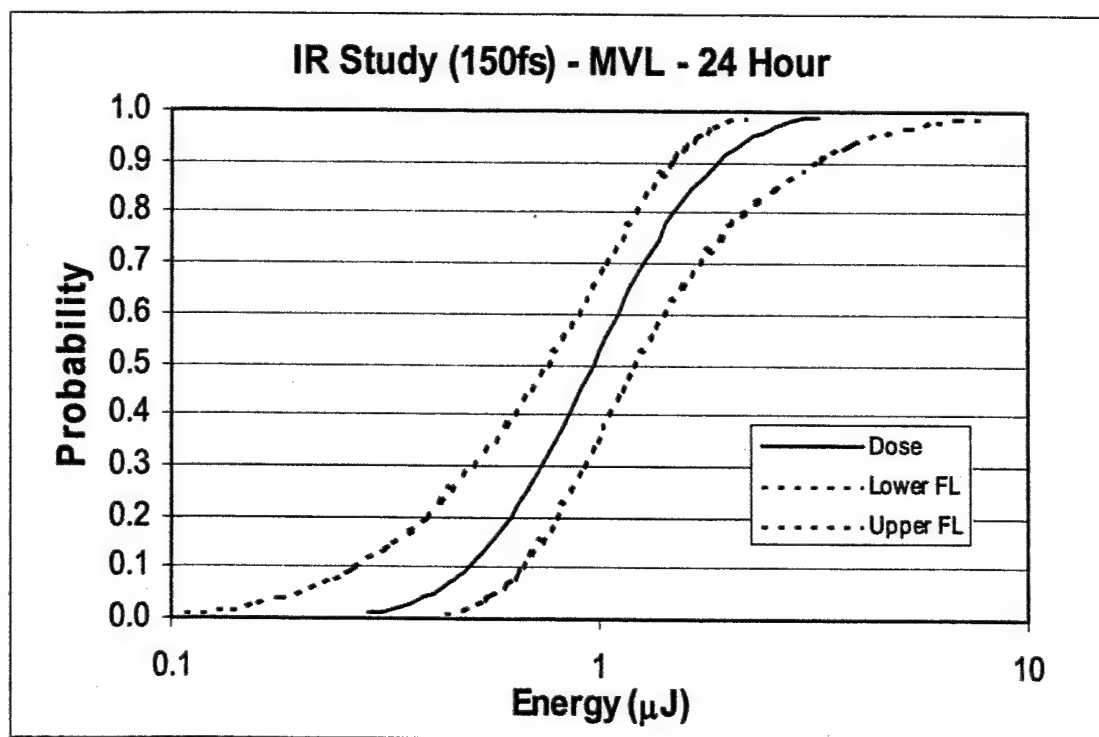
Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.00200		1	0	1.05	1	1	2.55	1
0.120	1	0	1.16	1	0	2.60	1	1
0.180	1	0	1.19	1	0	2.61	1	1
0.210	1	0	1.22	1	1	2.96	1	1
0.350	1	0	1.25	1	1	3.00	1	1

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.380	2	0	1.28	1	1	3.73	1	1
0.400	2	0	1.30	2	2	3.90	1	1
0.420	1	0	1.38	1	0	4.10	1	1
0.500	1	0	1.40	1	1	4.29	1	1
0.510	1	1	1.44	1	0	4.76	1	1
0.520	2	0	1.50	1	1	6.00	1	1
0.530	2	0	1.51	1	1	6.83	1	1
0.580	1	0	1.61	1	1	7.10	1	1
0.640	1	0	1.64	1	0	7.13	1	1
0.690	1	0	1.67	1	1	8.35	1	1
0.700	1	0	1.81	1	1	8.40	1	1
0.730	1	1	1.85	1	1	8.70	1	1
0.740	1	0	1.90	1	0	10.9	1	1
0.770	1	1	1.97	1	1	11.4	1	1
0.780	1	0	2.02	1	1	11.7	1	1
0.810	1	0	2.11	1	1	12.5	2	2
0.950	2	1	2.12	1	1	13.4	1	1
0.970	1	1	2.17	1	1	13.7	1	1
1.02	1	1	2.48	1	1	13.9	1	1
1.03	1	1	2.51	1	1			

Totals

81

52



**IR Study (150fs) - FAVL - 1 Hour**  
A11 OS, A14 OS, C05 OD, C15 OS

ONES = 5      ZEROES = 76      TOTAL = 81

Percent confidence = 0.95

ED50 = 15.3    Upper FL = 263.      Lower FL = 9.24

Intercept = -3.40      Slope = 2.87

Pearson's Chi-Sq = 19.2979    Probability of Chi-Sq = 1.0000

h = 1.00      g = 0.63      t = 1.96

Log XBAR = 0.884    Log YBAR = 4.14

SYX = 25.407    SXY = 2.128    SXX = 0.741    S0 = 10.718

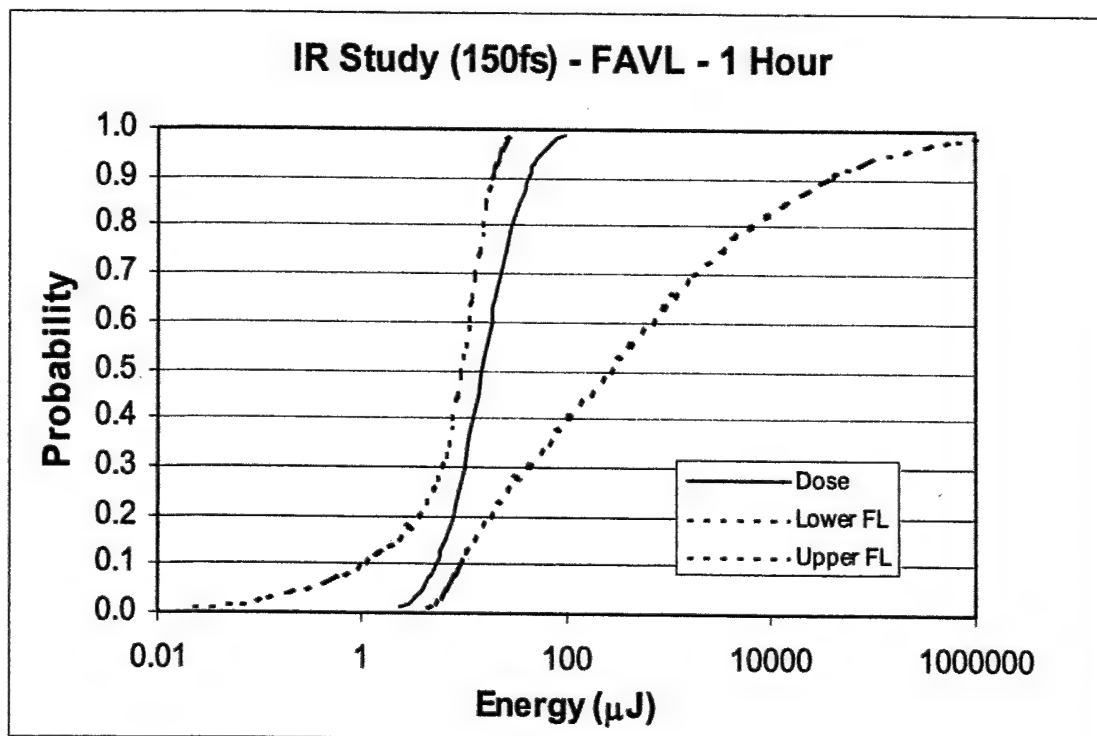
<u>Prob</u>	<u>Dose</u>	<u>LFL</u>	<u>UFL</u>	<u>Prob</u>	<u>Dose</u>	<u>LFL</u>	<u>UFL</u>
0.01	2.36	0.0232	4.49	0.55	16.9	10.0	418.
0.02	2.94	0.0651	5.20	0.60	18.7	10.8	673.
0.03	3.38	0.124	5.75	0.65	20.8	11.6	1.10e+003
0.04	3.75	0.201	6.23	0.70	23.3	12.5	1.87e+003
0.05	4.09	0.297	6.68	0.75	26.3	13.6	3.30e+003
0.06	4.39	0.411	7.12	0.80	30.0	14.8	6.24e+003
0.07	4.68	0.545	7.56	0.85	35.1	16.3	1.31e+004
0.08	4.95	0.698	8.01	0.90	42.7	18.4	3.36e+004
0.09	5.21	0.870	8.49	0.91	44.8	18.9	4.22e+004
0.10	5.47	1.06	8.98	0.92	47.2	19.5	5.40e+004
0.15	6.66	2.26	12.2	0.93	49.9	20.2	7.09e+004
0.20	7.78	3.63	17.6	0.94	53.2	21.0	9.60e+004
0.25	8.90	4.90	26.9	0.95	57.2	21.9	1.36e+005
0.30	10.0	5.97	42.1	0.96	62.2	23.0	2.04e+005
0.35	11.2	6.89	66.6	0.97	69.1	24.5	3.37e+005
0.40	12.5	7.72	105.	0.98	79.4	26.5	6.55e+005
0.45	13.8	8.49	166.	0.99	98.8	30.1	1.87e+006
0.50	15.3	9.24	263.				

<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	
0.00200		1	0	1.05	1	0	2.55	1	0
0.120	1	0	1.16	1	0	2.60	1	0	
0.180	1	0	1.19	1	0	2.61	1	0	
0.210	1	0	1.22	1	0	2.96	1	0	

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.350	1	0	1.25	1	0	3.00	1	0
0.380	2	0	1.28	1	0	3.73	1	0
0.400	2	0	1.30	2	0	3.90	1	0
0.420	1	0	1.38	1	0	4.10	1	0
0.500	1	0	1.40	1	0	4.29	1	0
0.510	1	0	1.44	1	0	4.76	1	0
0.520	2	0	1.50	1	0	6.00	1	0
0.530	2	0	1.51	1	0	6.83	1	1
0.580	1	0	1.61	1	0	7.10	1	0
0.640	1	0	1.64	1	0	7.13	1	1
0.690	1	0	1.67	1	0	8.35	1	0
0.700	1	0	1.81	1	0	8.40	1	0
0.730	1	0	1.85	1	0	8.70	1	1
0.740	1	0	1.90	1	0	10.9	1	0
0.770	1	0	1.97	1	0	11.4	1	0
0.780	1	0	2.02	1	0	11.7	1	0
0.810	1	0	2.11	1	0	12.5	2	1
0.950	2	0	2.12	1	0	13.4	1	0
0.970	1	0	2.17	1	0	13.7	1	1
1.02	1	0	2.48	1	0	13.9	1	0
1.03	1	0	2.51	1	0			

Totals

81 5



**IR Study (150fs) - FAVL - 24 Hour**  
**A11 OS, A14 OS, C05 OD, C15 OS**

ONES = 5      ZEROES = 76      TOTAL = 81

Percent confidence = 0.95

ED50 = 12.2    Upper FL = 1.77e+031      Lower FL = 8.77

Intercept = -6.08      Slope = 5.60

Pearson's Chi-Sq = 17.1397    Probability of Chi-Sq = 1.0000

h = 1.00      g = 1.00      t = 1.96

Log XBAR = 1.01    Log YBAR = 4.59

SYX = 21.000    SXY = 0.690    SXX = 0.123    S0 = 7.828

Prob	Dose	Lower FL	Upper FL	Prob	Dose	Lower FL	Upper FL
0.01	4.68	7.10e-140	7.32	0.55	12.8	9.53	2.63e+040
0.02	5.24	6.30e-120	7.81	0.60	13.5	10.1	5.63e+049
0.03	5.62	2.85e-107	8.15	0.65	14.3	10.7	2.50e+059
0.04	5.93	9.43e-098	8.43	0.70	15.1	11.2	3.71e+069
0.05	6.20	5.22e-090	8.67	0.75	16.1	11.7	3.54e+080
0.06	6.43	2.03e-083	8.89	0.80	17.2	12.3	5.97e+092
0.07	6.65	1.22e-077	9.09	0.85	18.7	12.9	1.07e+107
0.08	6.84	1.82e-072	9.29	0.90	20.7	13.7	9.24e+124
0.09	7.02	9.19e-068	9.48	0.91	21.2	13.9	1.98e+129
0.10	7.20	1.97e-063	9.67	0.92	21.7	14.2	1.01e+134
0.15	7.96	1.64e-045	10.6	0.93	22.4	14.4	1.51e+139
0.20	8.63	2.76e-031	11.9	0.94	23.1	14.7	9.10e+144
0.25	9.24	4.07e-019	14.3	0.95	24.0	15.0	3.56e+151
0.30	9.83	2.44e-008	23.7	0.96	25.1	15.3	1.98e+159
0.35	10.4	0.877	1.03e+004	0.97	26.4	15.8	6.57e+168
0.40	11.0	5.70	7.42e+012	0.98	28.4	16.4	2.99e+181
0.45	11.6	7.69	1.25e+022	0.99	31.8	17.4	2.66e+201
0.50	12.2	8.77	1.77e+031				

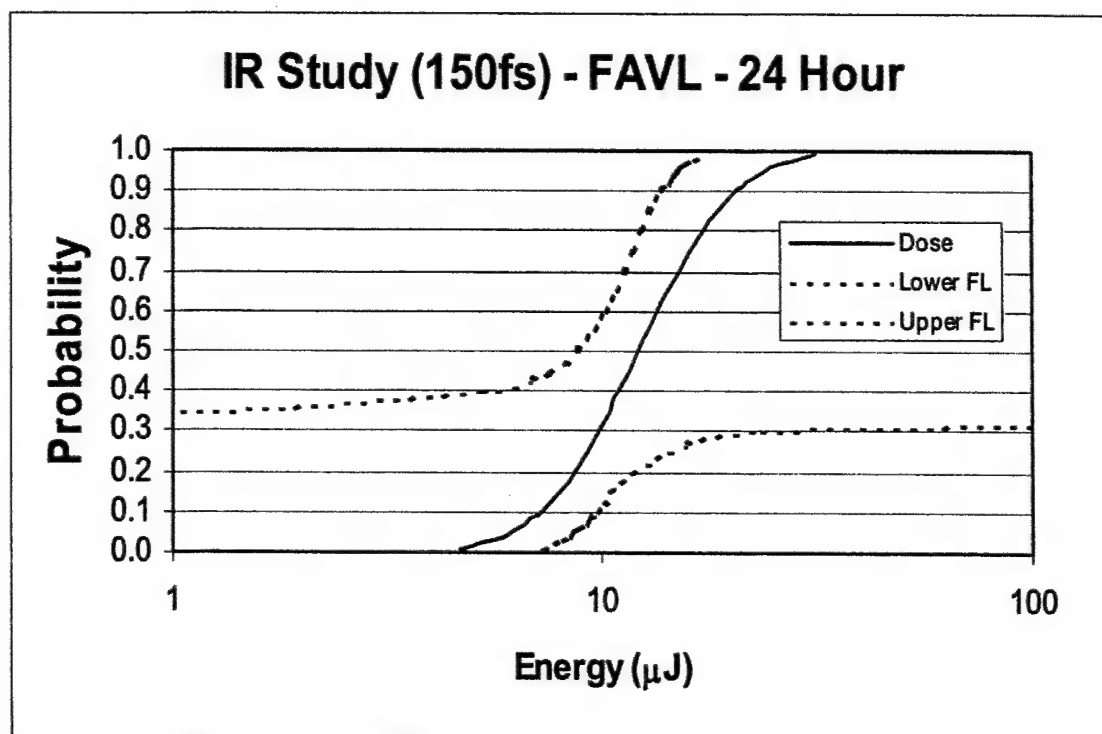
Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.00200		1	0	1.05	1	0	2.55	1
0.120	1	0	1.16	1	0	2.60	1	0
0.180	1	0	1.19	1	0	2.61	1	0
0.210	1	0	1.22	1	0	2.96	1	0
0.350	1	0	1.25	1	0	3.00	1	0

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.380	2	0	1.28	1	0	3.73	1	0
0.400	2	0	1.30	2	0	3.90	1	0
0.420	1	0	1.38	1	0	4.10	1	0
0.500	1	0	1.40	1	0	4.29	1	0
0.510	1	0	1.44	1	0	4.76	1	0
0.520	2	0	1.50	1	0	6.00	1	0
0.530	2	0	1.51	1	0	6.83	1	0
0.580	1	0	1.61	1	0	7.10	1	0
0.640	1	0	1.64	1	0	7.13	1	1
0.690	1	0	1.67	1	0	8.35	1	0
0.700	1	0	1.81	1	0	8.40	1	0
0.730	1	0	1.85	1	0	8.70	1	0
0.740	1	0	1.90	1	0	10.9	1	0
0.770	1	0	1.97	1	0	11.4	1	0
0.780	1	0	2.02	1	0	11.7	1	0
0.810	1	0	2.11	1	0	12.5	2	2
0.950	2	0	2.12	1	0	13.4	1	0
0.970	1	0	2.17	1	0	13.7	1	1
1.02	1	0	2.48	1	0	13.9	1	1
1.03	1	0	2.51	1	0			

Totals

81

5



**IR Study (100fs) - MVL - 1 Hour**  
**C47 OD, C47 OD, B60 OD, B60 OS**

ONES = 28    ZEROES = 35    TOTAL = 63

Percent confidence = 0.95

ED50 = 0.361 Upper FL = 0.627    Lower FL = 0.223

Intercept = 0.837    Slope = 1.89

Pearson's Chi-Sq = 40.9176    Probability of Chi-Sq = 0.5620

h = 1.00    g = 0.23    t = 1.96

Log XBAR = -0.496    Log YBAR = 4.90

SY Y = 57.927 SXY = 8.992    SXX = 4.754    S0 = 28.189

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.0213	0.00170	0.0549	0.55	0.421	0.266	0.781
0.02	0.0296	0.00316	0.0695	0.60	0.491	0.314	0.991
0.03	0.0366	0.00468	0.0808	0.65	0.577	0.366	1.28
0.04	0.0429	0.00629	0.0906	0.70	0.684	0.427	1.71
0.05	0.0488	0.00799	0.0995	0.75	0.821	0.499	2.34
0.06	0.0544	0.00978	0.108	0.80	1.01	0.589	3.36
0.07	0.0599	0.0117	0.116	0.85	1.27	0.708	5.15
0.08	0.0653	0.0137	0.123	0.90	1.72	0.886	8.90
0.09	0.0706	0.0158	0.131	0.91	1.85	0.935	10.2
0.10	0.0759	0.0180	0.138	0.92	2.00	0.990	11.7
0.15	0.102	0.0309	0.174	0.93	2.18	1.05	13.8
0.20	0.130	0.0470	0.212	0.94	2.40	1.13	16.5
0.25	0.159	0.0666	0.252	0.95	2.67	1.22	20.2
0.30	0.191	0.0900	0.299	0.96	3.04	1.34	25.7
0.35	0.226	0.118	0.355	0.97	3.56	1.50	34.5
0.40	0.265	0.149	0.424	0.98	4.40	1.75	51.3
0.45	0.310	0.184	0.512	0.99	6.13	2.20	95.6
0.50	0.361	0.223	0.627				

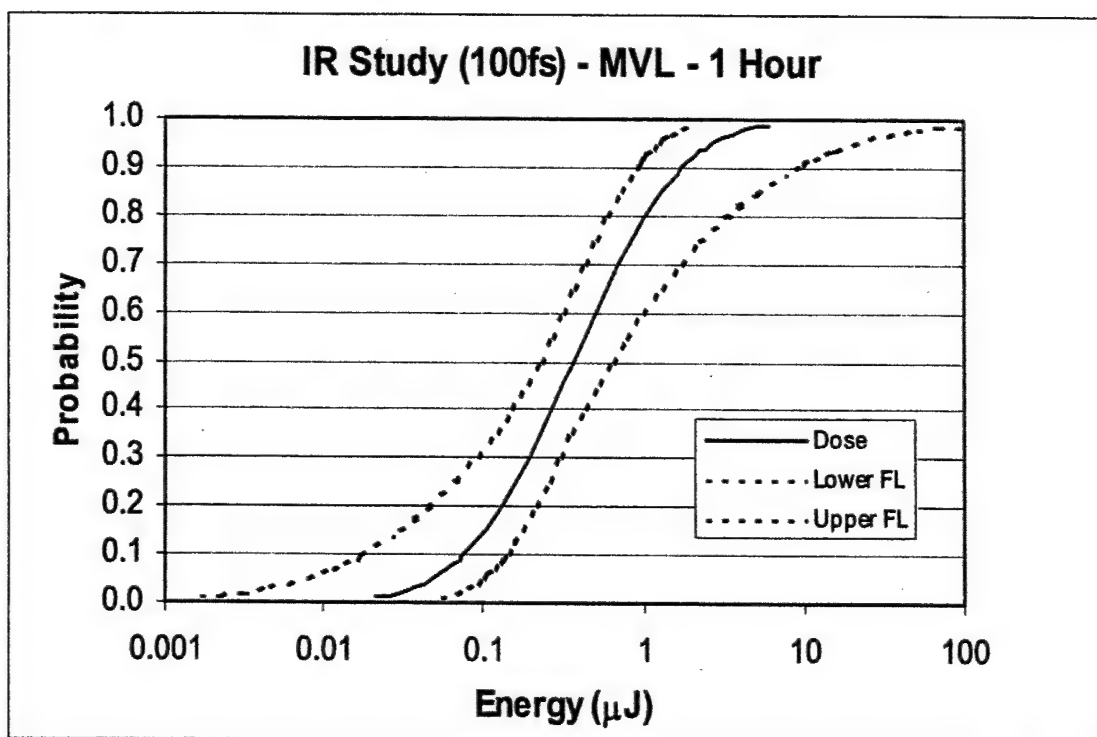
Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0100	1	0	0.250	2	1	0.690	1	1
0.0200	2	0	0.260	1	1	0.700	1	1
0.0300	2	0	0.270	1	0	0.840	1	0
0.0500	4	1	0.300	2	0	0.900	1	1
0.0700	1	0	0.380	1	1	1.00	1	1

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0800	4	0	0.390	1	1	1.05	1	1
0.0900	2	1	0.400	1	0	1.10	1	1
0.100	1	0	0.420	1	1	1.11	1	1
0.110	1	0	0.460	1	0	1.72	1	1
0.140	2	0	0.480	1	1	1.89	1	1
0.170	1	0	0.560	1	1	2.04	1	0
0.190	1	0	0.580	2	1	2.27	1	1
0.200	2	1	0.640	1	1	5.45	1	1
0.230	2	0	0.660	1	1	8.00	1	1
0.240	3	0	0.670	2	2	18.0	1	1

Totals

63

28





**IR Study (100fs) - MVL - 24 Hour**  
**C47 OD, C47 OD, B60 OD, B60 OS**

ONES = 40    ZEROES = 23    TOTAL = 63

Percent confidence = 0.95

ED50 = 0.162    Upper FL = 0.229    Lower FL = 0.104

Intercept = 2.36    Slope = 2.98

Pearson's Chi-Sq = 27.9290    Probability of Chi-Sq = 0.9635

h = 1.00    g = 0.20    t = 1.96

Log XBAR = -0.710    Log YBAR = 5.24

SYX = 46.992    SXY = 6.389    SXX = 2.141    S0 = 19.946

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.0269	0.00504	0.0529	0.55	0.179	0.119	0.256
0.02	0.0332	0.00734	0.0616	0.60	0.197	0.135	0.289
0.03	0.0380	0.00930	0.0679	0.65	0.218	0.153	0.330
0.04	0.0420	0.0111	0.0731	0.70	0.243	0.172	0.383
0.05	0.0456	0.0128	0.0777	0.75	0.273	0.194	0.454
0.06	0.0488	0.0145	0.0818	0.80	0.310	0.220	0.553
0.07	0.0519	0.0161	0.0857	0.85	0.361	0.252	0.704
0.08	0.0548	0.0178	0.0893	0.90	0.436	0.296	0.964
0.09	0.0576	0.0194	0.0927	0.91	0.456	0.307	1.04
0.10	0.0603	0.0210	0.0960	0.92	0.479	0.320	1.13
0.15	0.0729	0.0291	0.111	0.93	0.506	0.334	1.24
0.20	0.0847	0.0376	0.125	0.94	0.538	0.350	1.38
0.25	0.0963	0.0466	0.140	0.95	0.577	0.370	1.56
0.30	0.108	0.0564	0.154	0.96	0.626	0.394	1.79
0.35	0.120	0.0669	0.170	0.97	0.692	0.425	2.14
0.40	0.133	0.0784	0.187	0.98	0.791	0.470	2.70
0.45	0.147	0.0909	0.207	0.99	0.976	0.549	3.91
0.50	0.162	0.104	0.229				

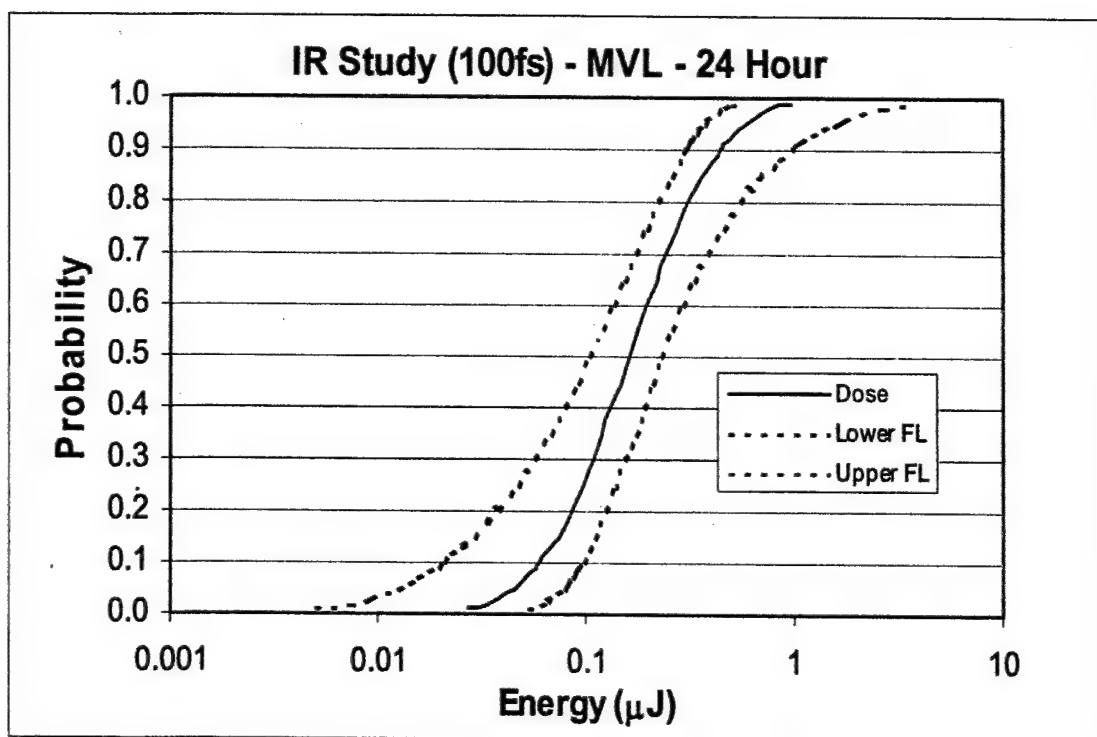
Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0100	1	0	0.250	2	1	0.690	1	1
0.0200	2	0	0.260	1	1	0.700	1	1
0.0300	2	0	0.270	1	0	0.840	1	1
0.0500	4	0	0.300	2	2	0.900	1	1
0.0700	1	1	0.380	1	1	1.00	1	1

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0800	4	1	0.390	1	1	1.05	1	1
0.0900	2	0	0.400	1	0	1.10	1	1
0.100	1	1	0.420	1	1	1.11	1	1
0.110	1	0	0.460	1	1	1.72	1	1
0.140	2	0	0.480	1	1	1.89	1	1
0.170	1	0	0.560	1	1	2.04	1	1
0.190	1	1	0.580	2	2	2.27	1	1
0.200	2	2	0.640	1	1	5.45	1	1
0.230	2	1	0.660	1	1	8.00	1	1
0.240	3	2	0.670	2	2	18.0	1	1

Totals

63

40



**Spotsize Study (+0.75 Diopter) - MVL - 1hr**  
**C63 OS, C65 OD**

ONES = 12                      ZEROES = 38                      TOTAL = 50

Percent confidence = 0.95

ED50 = 2.25    Upper FL = 10.4            Lower FL = 1.23

Intercept =      1.07    Slope = 3.04

Pearson's Chi-Sq = 88.9048    Probability of Chi-Sq = 0.0001

h = 1.98            g = 0.62            t = 2.01

Log XBAR = 0.228    Log YBAR = 4.62

SY Y = 101.837            SXY = 4.260    SXX = 1.403    S0 = 15.427

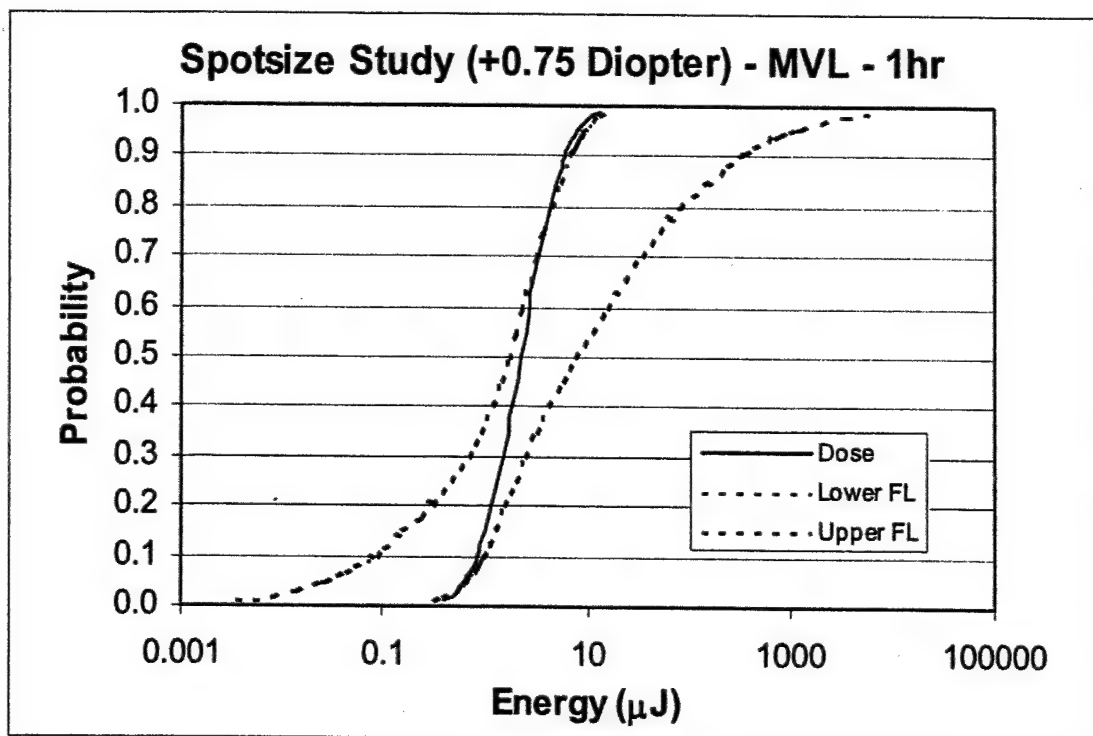
Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.385	0.00358	0.334	0.55	2.48	1.98	10.7
0.02	0.474	0.00825	0.430	0.60	2.73	2.31	15.3
0.03	0.540	0.0140	0.507	0.65	3.01	2.68	22.3
0.04	0.596	0.0207	0.574	0.70	3.35	3.11	33.4
0.05	0.646	0.0285	0.635	0.75	3.75	3.63	52.1
0.06	0.692	0.0374	0.694	0.80	4.26	4.29	86.0
0.07	0.735	0.0474	0.751	0.85	4.94	5.18	155.
0.08	0.775	0.0586	0.806	0.90	5.95	6.53	326.
0.09	0.814	0.0709	0.861	0.91	6.22	6.90	391.
0.10	0.851	0.0844	0.916	0.92	6.53	7.32	476.
0.15	1.03	0.172	1.20	0.93	6.89	7.82	591.
0.20	1.19	0.295	1.51	0.94	7.32	8.41	753.
0.25	1.35	0.457	1.90	0.95	7.84	9.14	993.
0.30	1.51	0.656	2.42	0.96	8.49	10.1	1.37e+003
0.35	1.68	0.884	3.12	0.97	9.37	11.3	2.05e+003
0.40	1.86	1.13	4.12	0.98	10.7	13.3	3.50e+003
0.45	2.05	1.40	5.56	0.99	13.1	17.0	8.11e+003
0.50	2.25	1.68	7.64				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0300	1	0	0.570	1	0	1.71	1	0
0.0800	1	0	0.680	1	0	1.82	1	0
0.0900	1	0	0.730	1	0	1.84	1	0
0.100	1	0	0.770	1	0	2.21	1	1
0.110	1	0	0.790	1	0	2.23	1	0

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.210	1	0	0.830	1	0	2.38	1	1
0.220	1	0	0.840	1	0	3.29	1	0
0.240	2	0	0.920	2	0	3.43	1	1
0.260	2	0	0.960	1	0	3.56	1	1
0.330	1	0	1.04	1	0	3.78	1	1
0.350	1	0	1.06	1	0	4.10	1	1
0.370	1	0	1.13	1	0	4.48	1	1
0.420	1	1	1.23	1	1	4.69	1	1
0.520	1	0	1.36	1	0	6.84	1	1
0.540	1	0	1.40	1	0	7.30	1	1
0.550	1	0	1.58	1	0			

**Totals**

**50 12**



**Spotsize Study (+0.75 Diopter) - MVL - 24hr**  
**C63 OS, C65 OD**

ONES = 22                      ZEROES = 28                      TOTAL = 50

Percent confidence = 0.95

ED50 = 1.04    Upper FL = 1.77                      Lower FL = 0.634

Intercept =      0.0371                      Slope = 2.17

Pearson's Chi-Sq = 48.4574    Probability of Chi-Sq = 0.3353

h = 1.00                      g = 0.26                      t = 1.96

Log XBAR = -0.00657                      Log YBAR = 4.95

SYX = 62.982 SXY = 6.682    SXX = 3.074    S0 = 22.287

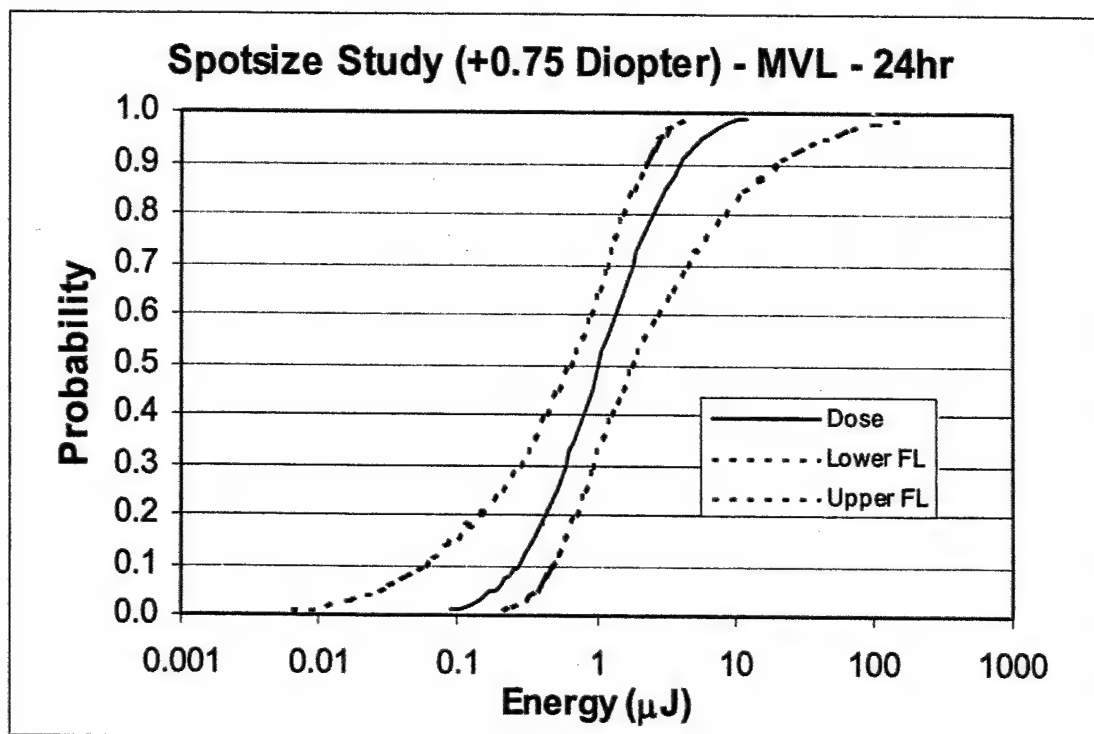
<u>Prob</u>	<u>Dose</u>	<u>LFL</u>	<u>UFL</u>	<u>Prob</u>	<u>Dose</u>	<u>LFL</u>	<u>UFL</u>
0.01	0.0885	0.00639	0.216	0.55	1.19	0.749	2.16
0.02	0.118	0.0115	0.265	0.60	1.36	0.872	2.68
0.03	0.142	0.0166	0.301	0.65	1.56	1.01	3.39
0.04	0.163	0.0219	0.332	0.70	1.81	1.16	4.40
0.05	0.182	0.0274	0.359	0.75	2.13	1.33	5.89
0.06	0.200	0.0332	0.385	0.80	2.54	1.54	8.23
0.07	0.218	0.0392	0.409	0.85	3.12	1.82	12.3
0.08	0.235	0.0455	0.432	0.90	4.04	2.21	20.4
0.09	0.251	0.0520	0.455	0.91	4.30	2.31	23.1
0.10	0.268	0.0589	0.477	0.92	4.61	2.43	26.5
0.15	0.347	0.0977	0.582	0.93	4.97	2.57	30.8
0.20	0.426	0.145	0.687	0.94	5.40	2.73	36.4
0.25	0.509	0.201	0.800	0.95	5.94	2.92	44.0
0.30	0.597	0.268	0.927	0.96	6.64	3.16	55.2
0.35	0.692	0.345	1.08	0.97	7.63	3.48	72.8
0.40	0.795	0.432	1.26	0.98	9.16	3.96	105.
0.45	0.910	0.528	1.48	0.99	12.2	4.83	189.
0.50	1.04	0.634	1.77				

<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>
0.0300	1	0	0.570	1	0	1.71	1	1
0.0800	1	0	0.680	1	0	1.82	1	0
0.0900	1	0	0.730	1	0	1.84	1	1
0.100	1	0	0.770	1	0	2.21	1	1
0.110	1	0	0.790	1	0	2.23	1	1

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.210	1	1	0.830	1	0	2.38	1	1
0.220	1	0	0.840	1	1	3.29	1	1
0.240	2	0	0.920	2	0	3.43	1	1
0.260	2	0	0.960	1	0	3.56	1	1
0.330	1	1	1.04	1	0	3.78	1	1
0.350	1	0	1.06	1	0	4.10	1	1
0.370	1	0	1.13	1	0	4.48	1	1
0.420	1	1	1.23	1	1	4.69	1	1
0.520	1	0	1.36	1	1	6.84	1	1
0.540	1	0	1.40	1	1	7.30	1	1
0.550	1	1	1.58	1	0			

Totals

50 22



Spotsize Study (No lens) - MVL - 1hr  
A11 OS, A14 OS, C05 OD, C15 OS

ONES = 38                      ZEROES = 43                      TOTAL = 81

Percent confidence = 0.95

ED50 = 1.78    Upper FL = 2.67                      Lower FL = 1.23

Intercept = -0.526      Slope = 2.11

Pearson's Chi-Sq = 68.5424    Probability of Chi-Sq = 0.5937

h = 1.00                      g = 0.17                      t = 1.96

Log XBAR = 0.201    Log YBAR = 4.90

SYX = 91.547 SXY = 10.904 SXX = 5.169    S0 = 37.331

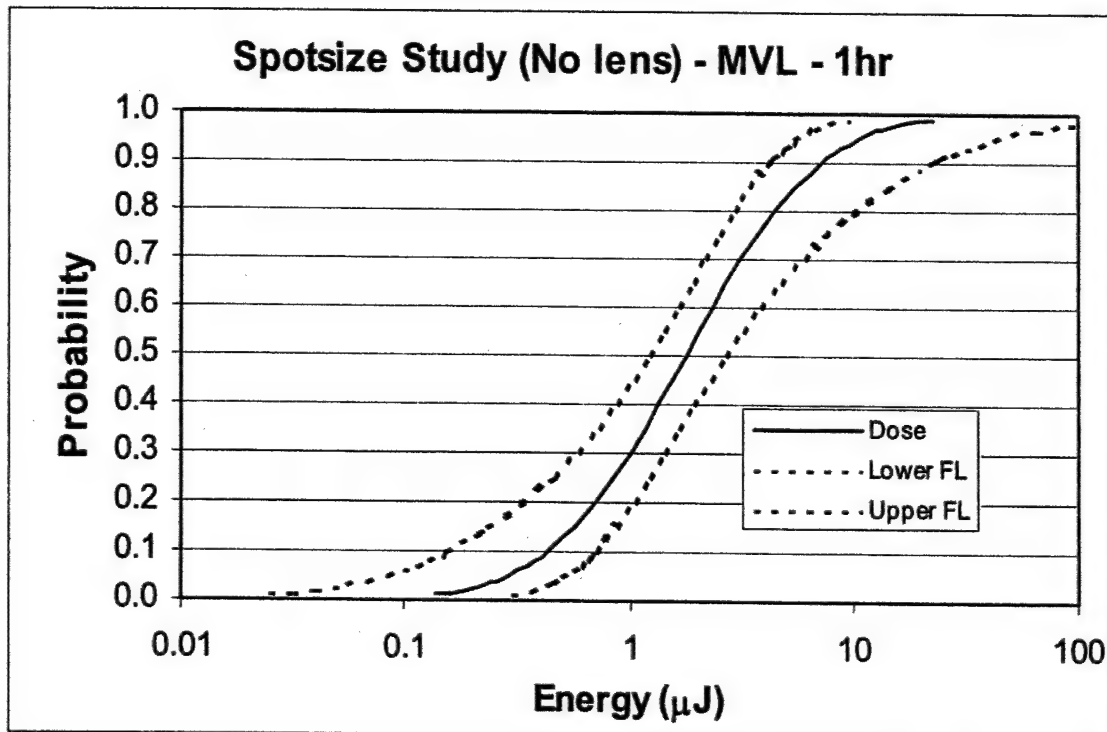
Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.140	0.0246	0.301	0.55	2.04	1.43	3.20
0.02	0.189	0.0404	0.375	0.60	2.34	1.65	3.88
0.03	0.228	0.0553	0.431	0.65	2.70	1.89	4.78
0.04	0.263	0.0699	0.480	0.70	3.15	2.17	6.01
0.05	0.295	0.0846	0.523	0.75	3.71	2.50	7.73
0.06	0.325	0.0994	0.564	0.80	4.45	2.90	10.3
0.07	0.355	0.114	0.602	0.85	5.50	3.44	14.5
0.08	0.383	0.130	0.639	0.90	7.19	4.23	22.4
0.09	0.411	0.146	0.674	0.91	7.67	4.44	24.9
0.10	0.438	0.162	0.709	0.92	8.23	4.68	28.0
0.15	0.573	0.248	0.877	0.93	8.89	4.97	31.7
0.20	0.709	0.347	1.05	0.94	9.69	5.30	36.6
0.25	0.850	0.459	1.23	0.95	10.7	5.70	43.0
0.30	1.00	0.585	1.43	0.96	12.0	6.21	52.1
0.35	1.17	0.725	1.66	0.97	13.8	6.90	66.0
0.40	1.35	0.880	1.93	0.98	16.7	7.94	90.3
0.45	1.55	1.05	2.26	0.99	22.5	9.87	148.
0.50	1.78	1.23	2.67				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.00200		1	0	1.05	1	1	2.55	1
0.120	1	0	1.16	1	0	2.60	1	0
0.180	1	0	1.19	1	0	2.61	1	0
0.210	1	0	1.22	1	1	2.96	1	0
0.350	1	0	1.25	1	0	3.00	1	0

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.380	2	0	1.28	1	0	3.73	1	1
0.400	2	0	1.30	2	1	3.90	1	1
0.420	1	0	1.38	1	0	4.10	1	0
0.500	1	0	1.40	1	1	4.29	1	1
0.510	1	1	1.44	1	0	4.76	1	1
0.520	2	0	1.50	1	1	6.00	1	1
0.530	2	0	1.51	1	1	6.83	1	1
0.580	1	0	1.61	1	0	7.10	1	1
0.640	1	0	1.64	1	0	7.13	1	1
0.690	1	0	1.67	1	0	8.35	1	1
0.700	1	0	1.81	1	1	8.40	1	0
0.730	1	1	1.85	1	1	8.70	1	1
0.740	1	0	1.90	1	0	10.9	1	1
0.770	1	0	1.97	1	1	11.4	1	1
0.780	1	0	2.02	1	1	11.7	1	1
0.810	1	0	2.11	1	1	12.5	2	2
0.950	2	1	2.12	1	0	13.4	1	1
0.970	1	0	2.17	1	1	13.7	1	1
1.02	1	1	2.48	1	1	13.9	1	1
1.03	1	1	2.51	1	1			

Totals

81 38





# Spotsize Study (No lens) - MVL - 24hr

A11 OS, A14 OS, C05 OD, C15 OS

ONES = 52    ZEROES = 29    TOTAL = 81

Percent confidence = 0.95

ED50 = 0.969    Upper FL = 1.20    Lower FL = 0.754

Intercept = 0.0598    Slope = 4.42

Pearson's Chi-Sq = 48.5680    Probability of Chi-Sq = 0.9846

h = 1.00    g = 0.18    t = 1.96

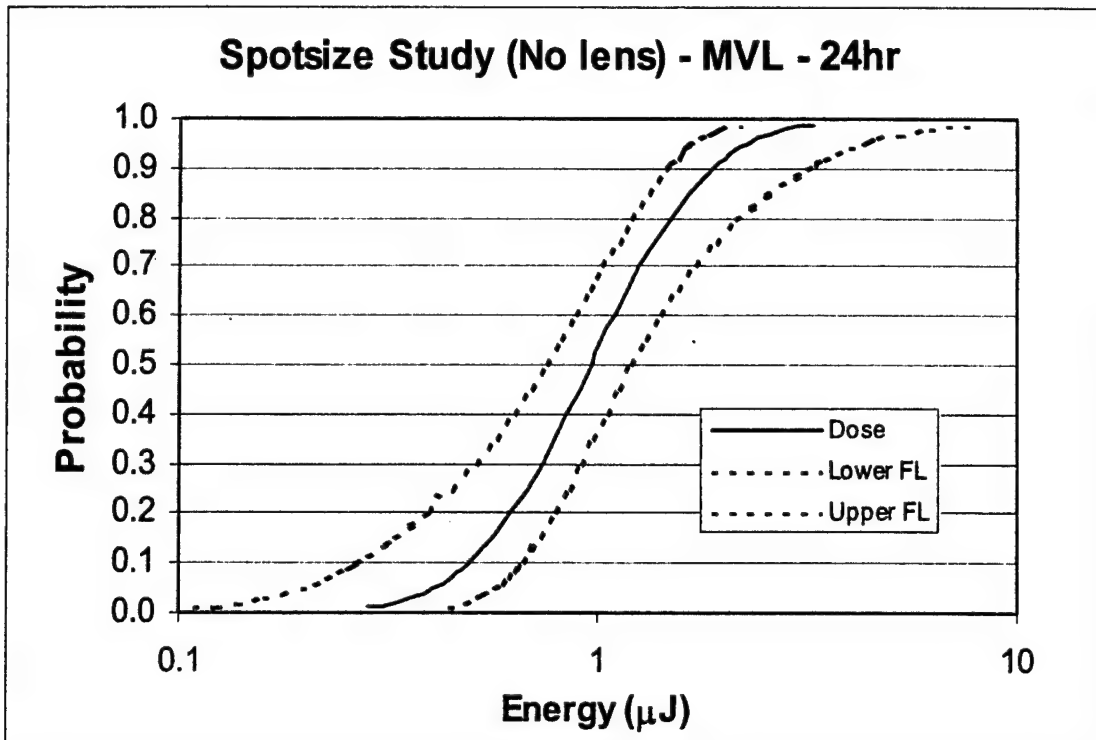
Log XBAR = 0.0199    Log YBAR = 5.15

SYX = 70.159    SXY = 4.888    SXX = 1.107    S0 = 23.812

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.288	0.108	0.439	0.55	1.03	0.819	1.30
0.02	0.332	0.138	0.488	0.60	1.11	0.887	1.41
0.03	0.364	0.160	0.522	0.65	1.18	0.958	1.55
0.04	0.389	0.180	0.549	0.70	1.27	1.03	1.71
0.05	0.411	0.197	0.572	0.75	1.38	1.12	1.92
0.06	0.431	0.213	0.593	0.80	1.50	1.21	2.19
0.07	0.449	0.229	0.612	0.85	1.66	1.32	2.56
0.08	0.466	0.243	0.629	0.90	1.89	1.47	3.15
0.09	0.482	0.257	0.645	0.91	1.95	1.50	3.31
0.10	0.497	0.271	0.661	0.92	2.02	1.55	3.49
0.15	0.565	0.334	0.731	0.93	2.09	1.59	3.71
0.20	0.625	0.393	0.794	0.94	2.18	1.64	3.97
0.25	0.682	0.452	0.855	0.95	2.28	1.70	4.30
0.30	0.737	0.510	0.916	0.96	2.41	1.78	4.71
0.35	0.793	0.569	0.979	0.97	2.58	1.87	5.27
0.40	0.849	0.629	1.05	0.98	2.83	2.00	6.14
0.45	0.908	0.691	1.12	0.99	3.26	2.23	7.80
0.50	0.969	0.754	1.20				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.00200		1	0	1.05	1	1	2.55	1
0.120	1	0	1.16	1	0	2.60	1	1
0.180	1	0	1.19	1	0	2.61	1	1
0.210	1	0	1.22	1	1	2.96	1	1
0.350	1	0	1.25	1	1	3.00	1	1

<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>
0.380	2	0	1.28	1	1	3.73	1	1
0.400	2	0	1.30	2	2	3.90	1	1
0.420	1	0	1.38	1	0	4.10	1	1
0.500	1	0	1.40	1	1	4.29	1	1
0.510	1	1	1.44	1	0	4.76	1	1
0.520	2	0	1.50	1	1	6.00	1	1
0.530	2	0	1.51	1	1	6.83	1	1
0.580	1	0	1.61	1	1	7.10	1	1
0.640	1	0	1.64	1	0	7.13	1	1
0.690	1	0	1.67	1	1	8.35	1	1
0.700	1	0	1.81	1	1	8.40	1	1
0.730	1	1	1.85	1	1	8.70	1	1
0.740	1	0	1.90	1	0	10.9	1	1
0.770	1	1	1.97	1	1	11.4	1	1
0.780	1	0	2.02	1	1	11.7	1	1
0.810	1	0	2.11	1	1	12.5	2	2
0.950	2	1	2.12	1	1	13.4	1	1
0.970	1	1	2.17	1	1	13.7	1	1
1.02	1	1	2.48	1	1	13.9	1	1
1.03	1	1	2.51	1	1			
<b>Totals</b>							<b>81</b>	<b>52</b>



# **Spotsize Study (No lens) - FAVL - 1hr**

A11 OS, A14 OS, C05 OD, C15 OS

ONES = 5      ZEROES = 76      TOTAL = 81

Percent confidence = 0.95

ED50 = 15.3    Upper FL = 263.      Lower FL = 9.24

Intercept = -3.40      Slope = 2.87

Pearson's Chi-Sq = 19.2979    Probability of Chi-Sq = 1.0000

h = 1.00      g = 0.63      t = 1.96

Log XBAR = 0.884    Log YBAR = 4.14

SYY = 25.407 SXY = 2.128 SXX = 0.741 S0 = 10.718

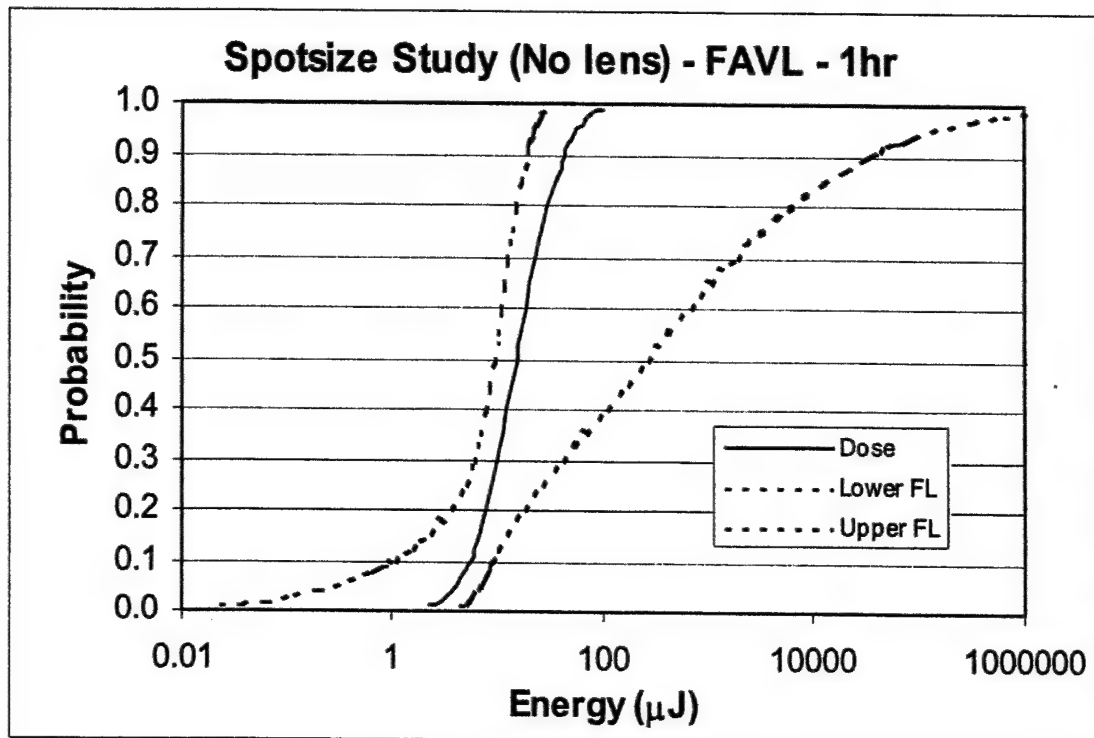
Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	2.36	0.0232	4.49	0.55	16.9	10.0	418.
0.02	2.94	0.0651	5.20	0.60	18.7	10.8	673.
0.03	3.38	0.124	5.75	0.65	20.8	11.6	1.10e+003
0.04	3.75	0.201	6.23	0.70	23.3	12.5	1.87e+003
0.05	4.09	0.297	6.68	0.75	26.3	13.6	3.30e+00
0.06	4.39	0.411	7.12	0.80	30.0	14.8	6.24e+003
0.07	4.68	0.545	7.56	0.85	35.1	16.3	1.31e+004
0.08	4.95	0.698	8.01	0.90	42.7	18.4	3.36e+004
0.09	5.21	0.870	8.49	0.91	44.8	18.9	4.22e+004
0.10	5.47	1.06	8.98	0.92	47.2	19.5	5.40e+00
0.15	6.66	2.26	12.2	0.93	49.9	20.2	7.09e+004
0.20	7.78	3.63	17.6	0.94	53.2	21.0	9.60e+004
0.25	8.90	4.90	26.9	0.95	57.2	21.9	1.36e+005
0.30	10.0	5.97	42.1	0.96	62.2	23.0	2.04e+005
0.35	11.2	6.89	66.6	0.97	69.1	24.5	3.37e+005
0.40	12.5	7.72	105.	0.98	79.4	26.5	6.55e+005
0.45	13.8	8.49	166.	0.99	98.8	30.1	1.87e+006
0.50	15.3	9.24	263.				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.00200	1	0	1.05	1	0	2.55	1	0
0.120	1	0	1.16	1	0	2.60	1	0
0.180	1	0	1.19	1	0	2.61	1	0
0.210	1	0	1.22	1	0	2.96	1	0
0.350	1	0	1.25	1	0	3.00	1	0

<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>
0.380	2	0	1.28	1	0	3.73	1	0
0.400	2	0	1.30	2	0	3.90	1	0
0.420	1	0	1.38	1	0	4.10	1	0
0.500	1	0	1.40	1	0	4.29	1	0
0.510	1	0	1.44	1	0	4.76	1	0
0.520	2	0	1.50	1	0	6.00	1	0
0.530	2	0	1.51	1	0	6.83	1	1
0.580	1	0	1.61	1	0	7.10	1	0
0.640	1	0	1.64	1	0	7.13	1	1
0.690	1	0	1.67	1	0	8.35	1	0
0.700	1	0	1.81	1	0	8.40	1	0
0.730	1	0	1.85	1	0	8.70	1	1
0.740	1	0	1.90	1	0	10.9	1	0
0.770	1	0	1.97	1	0	11.4	1	0
0.780	1	0	2.02	1	0	11.7	1	0
0.810	1	0	2.11	1	0	12.5	2	1
0.950	2	0	2.12	1	0	13.4	1	0
0.970	1	0	2.17	1	0	13.7	1	1
1.02	1	0	2.48	1	0	13.9	1	0
1.03	1	0	2.51	1	0			

**Totals**

**81 5**



**Spotsize Study (No lens) - FAVL - 24hr**  
A11 OS, A14 OS, C05 OD, C15 OS

ONES = 5      ZEROES = 76      TOTAL =      81

Percent confidence = 0.95

ED50 = 12.2    Upper FL = 1.77e+031      Lower FL = 8.77

Intercept = -6.08      Slope = 5.60

Pearson's Chi-Sq = 17.1397    Probability of Chi-Sq = 1.0000

h = 1.00      g = 1.00      t = 1.96

Log XBAR = 1.01    Log YBAR = 4.59

SYX = 21.000      SXY = 0.690    SXX = 0.123    S0 = 7.828

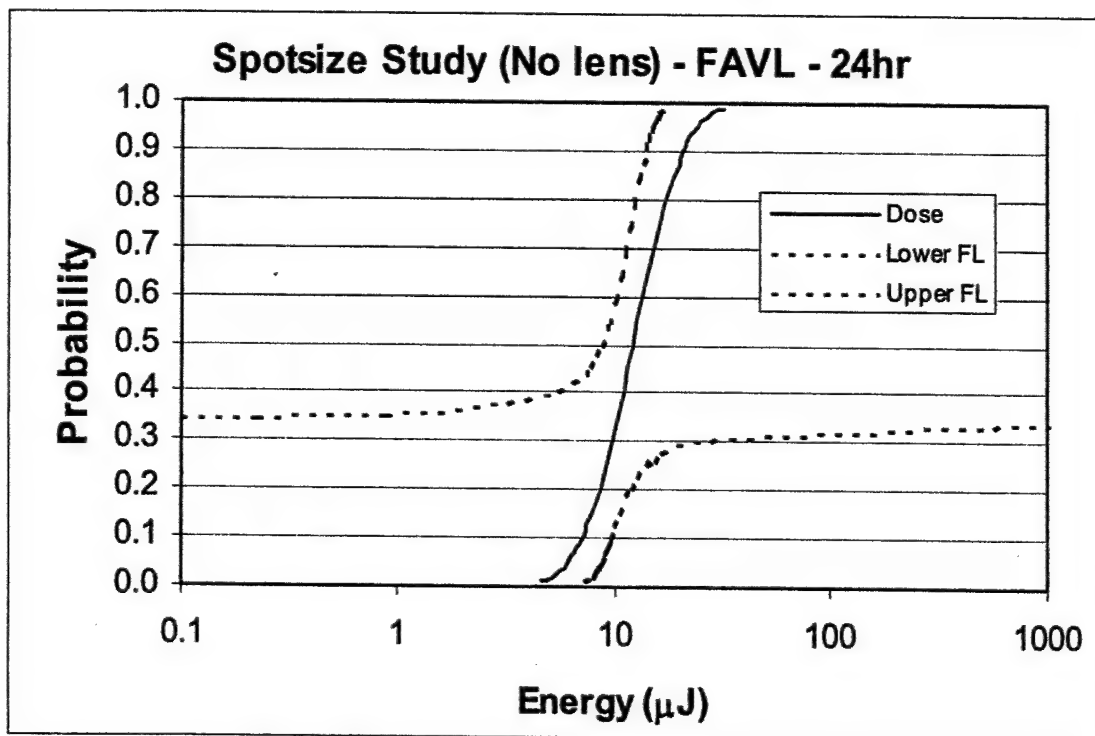
Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	4.68	7.10e-140	7.32	0.55	12.8	9.53	2.63e+040
0.02	5.24	6.30e-120	7.81	0.60	13.5	10.1	5.63e+049
0.03	5.62	2.85e-107	8.15	0.65	14.3	10.7	2.50e+059
0.04	5.93	9.43e-098	8.43	0.70	15.1	11.2	3.71e+069
0.05	6.20	5.22e-090	8.67	0.75	16.1	11.7	3.54e+080
0.06	6.43	2.03e-083	8.89	0.80	17.2	12.3	5.97e+092
0.07	6.65	1.22e-077	9.09	0.85	18.7	12.9	1.07e+107
0.08	6.84	1.82e-072	9.29	0.90	20.7	13.7	9.24e+124
0.09	7.02	9.19e-068	9.48	0.91	21.2	13.9	1.98e+129
0.10	7.20	1.97e-063	9.67	0.92	21.7	14.2	1.01e+134
0.15	7.96	1.64e-045	10.6	0.93	22.4	14.4	1.51e+139
0.20	8.63	2.76e-031	11.9	0.94	23.1	14.7	9.10e+144
0.25	9.24	4.07e-019	14.3	0.95	24.0	15.0	3.56e+151
0.30	9.83	2.44e-008	23.7	0.96	25.1	15.3	1.98e+159
0.35	10.4	0.877	1.03e+004	0.97	26.4	15.8	6.57e+168
0.40	11.0	5.70	7.42e+012	0.98	28.4	16.4	2.99e+181
0.45	11.6	7.69	1.25e+022	0.99	31.8	17.4	2.66e+201
0.50	12.2	8.77	1.77e+031				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.00200		1	0	1.05	1	0	2.55	1
0.120	1	0	1.16	1	0	2.60	1	0
0.180	1	0	1.19	1	0	2.61	1	0
0.210	1	0	1.22	1	0	2.96	1	0
0.350	1	0	1.25	1	0	3.00	1	0
0.380	2	0	1.28	1	0	3.73	1	0

<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>
0.400	2	0	1.30	2	0	3.90	1	0
0.420	1	0	1.38	1	0	4.10	1	0
0.500	1	0	1.40	1	0	4.29	1	0
0.510	1	0	1.44	1	0	4.76	1	0
0.520	2	0	1.50	1	0	6.00	1	0
0.530	2	0	1.51	1	0	6.83	1	0
0.580	1	0	1.61	1	0	7.10	1	0
0.640	1	0	1.64	1	0	7.13	1	1
0.690	1	0	1.67	1	0	8.35	1	0
0.700	1	0	1.81	1	0	8.40	1	0
0.730	1	0	1.85	1	0	8.70	1	0
0.740	1	0	1.90	1	0	10.9	1	0
0.770	1	0	1.97	1	0	11.4	1	0
0.780	1	0	2.02	1	0	11.7	1	0
0.810	1	0	2.11	1	0	12.5	2	2
0.950	2	0	2.12	1	0	13.4	1	0
0.970	1	0	2.17	1	0	13.7	1	1
1.02	1	0	2.48	1	0	13.9	1	1
1.03	1	0	2.51	1	0			

**Totals**

**81 5**





**Spotsize Study (-1 Diopter) - MVL -1hr**  
**A39 OS, C63 OD**

ONES = 21                      ZEROES = 29                      TOTAL = 50

Percent confidence = 0.95

ED50 = 3.24    Upper FL = 4.60                      Lower FL = 2.29

Intercept = -1.75                      Slope = 3.42

Pearson's Chi-Sq = 50.8450    Probability of Chi-Sq = 0.2543

h = 1.00                      g = 0.32                      t = 1.96

Log XBAR = 0.511                      Log YBAR = 5.00

SYX = 63.019    SXY = 3.559    SXX = 1.040    S0 = 20.985

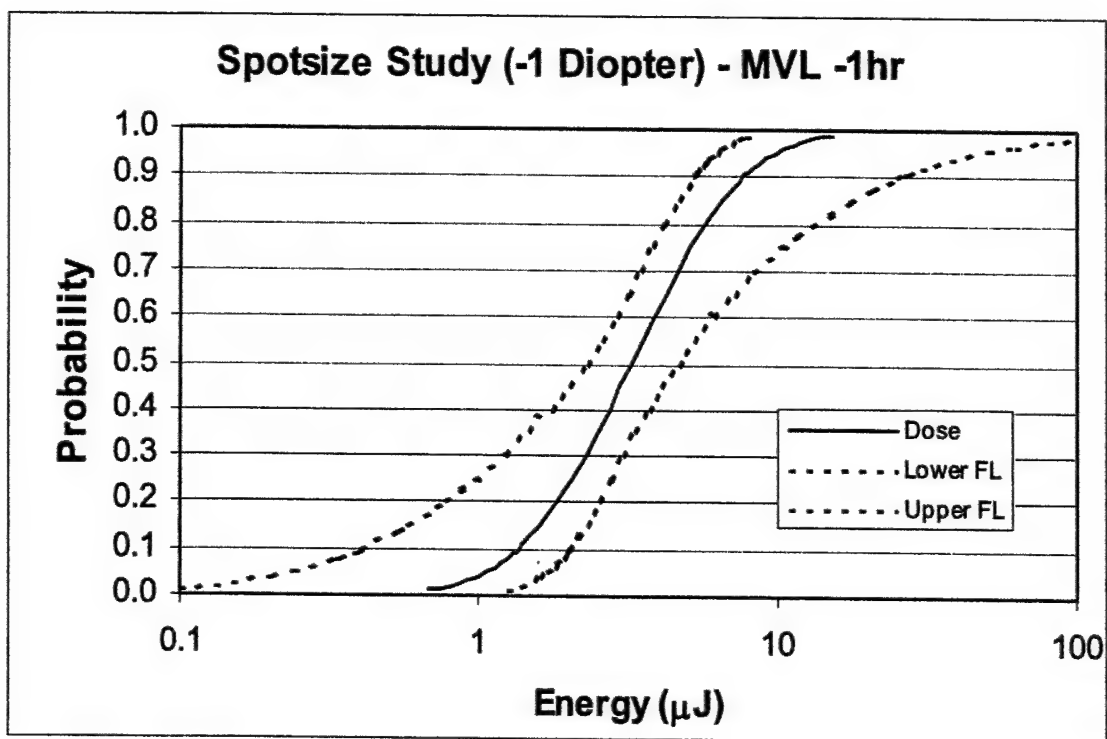
Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.678	0.0870	1.25	0.55	3.53	2.57	5.24
0.02	0.814	0.131	1.41	0.60	3.85	2.86	6.06
0.03	0.915	0.171	1.53	0.65	4.21	3.15	7.13
0.04	0.999	0.208	1.62	0.70	4.62	3.46	8.55
0.05	1.07	0.243	1.70	0.75	5.11	3.78	10.5
0.06	1.14	0.278	1.78	0.80	5.72	4.15	13.3
0.07	1.20	0.313	1.84	0.85	6.52	4.60	17.6
0.08	1.26	0.348	1.91	0.90	7.69	5.20	25.2
0.09	1.32	0.383	1.97	0.91	8.00	5.35	27.5
0.10	1.37	0.418	2.03	0.92	8.35	5.52	30.2
0.15	1.62	0.599	2.29	0.93	8.76	5.71	33.6
0.20	1.84	0.793	2.54	0.94	9.24	5.93	37.8
0.25	2.06	1.00	2.78	0.95	9.82	6.18	43.3
0.30	2.28	1.23	3.05	0.96	10.5	6.49	50.7
0.35	2.50	1.48	3.34	0.97	11.5	6.90	61.7
0.40	2.74	1.74	3.68	0.98	12.9	7.46	80.1
0.45	2.98	2.01	4.09	0.99	15.5	8.44	121.
0.50	3.24	2.29	4.60				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0100	1	0	2.18	1	1	4.19	1	1
0.340	1	0	2.25	1	0	4.48	1	1
0.350	2	0	2.40	1	0	4.63	1	0
0.520	1	0	2.49	1	0	4.72	1	1
0.540	1	0	2.66	1	0	4.88	1	1

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.760	1	0	3.13	1	0	4.90	1	1
0.960	2	0	3.18	1	0	5.15	1	0
0.970	1	0	3.20	1	0	5.17	2	2
1.02	1	1	3.25	1	0	5.71	1	1
1.16	1	0	3.26	1	1	6.30	1	1
1.34	1	0	3.29	1	0	6.50	1	1
1.45	1	0	3.37	1	0	6.80	1	1
1.63	1	0	3.75	1	1	7.30	1	1
1.70	1	0	3.76	1	1	11.8	1	1
1.76	1	0	3.78	1	0	24.6	1	1
2.00	1	1	4.13	1	1			

Totals

50 21



**Spotsize Study (-1 Diopter) - MVL -24hr**  
**A39 OS, C63 OD**

ONES = 28                      ZEROES = 22                      TOTAL = 50

Percent confidence = 0.95

ED50 = 2.13    Upper FL = 2.98                      Lower FL = 1.31

Intercept = -0.972                      Slope = 2.97

Pearson's Chi-Sq = 42.9861    Probability of Chi-Sq = 0.5576

h = 1.00                      g = 0.27                      t = 1.96

Log XBAR = 0.415                      Log YBAR = 5.26

SYX = 57.159    SXY = 4.776    SXX = 1.609    S0 = 21.328

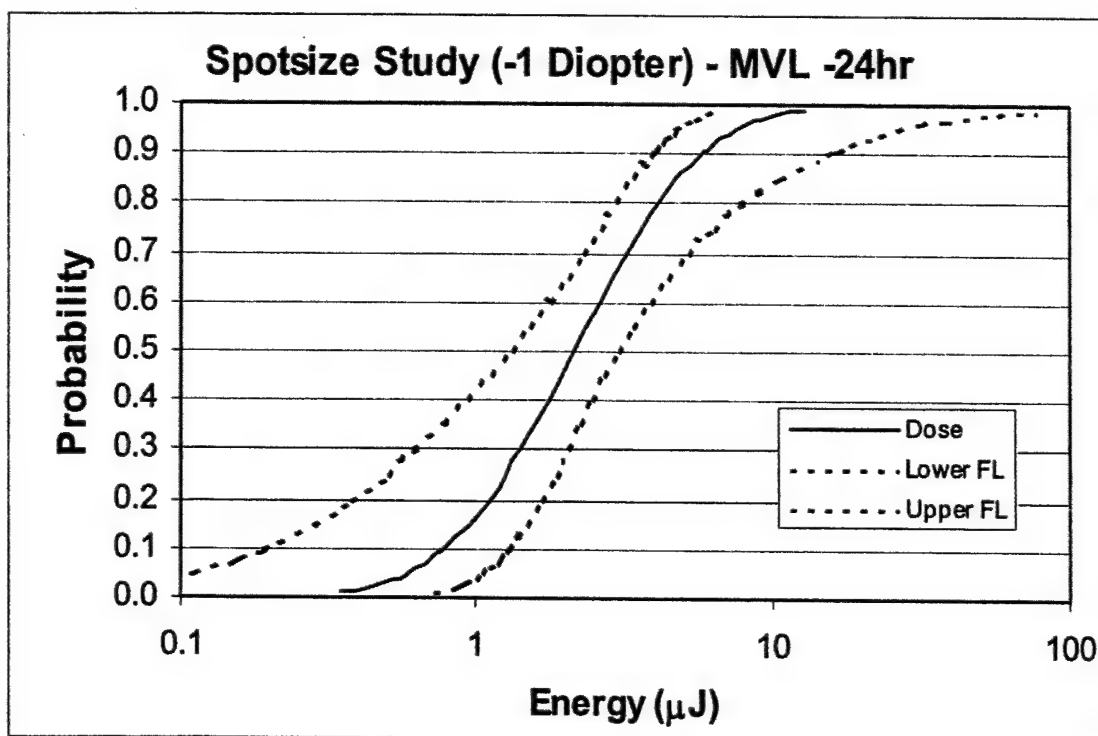
Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.350	0.0376	0.731	0.55	2.34	1.52	3.34
0.02	0.432	0.0582	0.845	0.60	2.59	1.76	3.80
0.03	0.494	0.0766	0.927	0.65	2.87	2.01	4.40
0.04	0.547	0.0942	0.995	0.70	3.19	2.28	5.21
0.05	0.593	0.111	1.05	0.75	3.59	2.58	6.34
0.06	0.636	0.129	1.11	0.80	4.09	2.92	7.99
0.07	0.677	0.146	1.16	0.85	4.75	3.34	10.6
0.08	0.715	0.163	1.20	0.90	5.75	3.89	15.3
0.09	0.751	0.180	1.25	0.91	6.02	4.03	16.8
0.10	0.787	0.198	1.29	0.92	6.32	4.19	18.5
0.15	0.951	0.290	1.48	0.93	6.68	4.36	20.6
0.20	1.11	0.392	1.66	0.94	7.10	4.57	23.3
0.25	1.26	0.505	1.83	0.95	7.62	4.81	26.8
0.30	1.42	0.632	2.02	0.96	8.27	5.11	31.7
0.35	1.58	0.774	2.21	0.97	9.15	5.49	38.8
0.40	1.75	0.933	2.43	0.98	10.5	6.04	51.0
0.45	1.93	1.11	2.68	0.99	12.9	7.01	78.6
0.50	2.13	1.31	2.98				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0100	1	0	2.18	1	0	4.19	1	1
0.340	1	0	2.25	1	1	4.48	1	1
0.350	2	0	2.40	1	0	4.63	1	1
0.520	1	0	2.49	1	0	4.72	1	1
0.540	1	0	2.66	1	1	4.88	1	1

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.760	1	1	3.13	1	1	4.90	1	1
0.960	2	0	3.18	1	0	5.15	1	1
0.970	1	0	3.20	1	0	5.17	2	2
1.02	1	1	3.25	1	1	5.71	1	1
1.16	1	0	3.26	1	1	6.30	1	1
1.34	1	0	3.29	1	0	6.50	1	1
1.45	1	0	3.37	1	0	6.80	1	1
1.63	1	1	3.75	1	0	7.30	1	1
1.70	1	0	3.76	1	1	11.8	1	1
1.76	1	0	3.78	1	1	24.6	1	1
2.00	1	1	4.13	1	1			

Totals

50 28



**Spotsize Study (-1 Diopter) - FAVL -1hr**  
**A39 OS, C63 OD**

ONES =15                      ZEROES = 35                      TOTAL = 50

Percent confidence = 0.95

ED50 = 5.53    Upper FL = 27.1            Lower FL = 3.38

Intercept = -1.39            Slope = 1.87

Pearson's Chi-Sq = 45.2384    Probability of Chi-Sq = 0.4620

h = 1.00            g = 0.52            t = 1.96

Log XBAR = 0.519                      Log YBAR = 4.58

SYX = 52.685    SXY = 3.988    SXX = 2.136    S0 = 24.078

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.314	0.000724	0.901	0.55	6.46	3.89	44.7
0.02	0.439	0.00236	1.11	0.60	7.56	4.42	75.4
0.03	0.544	0.00499	1.27	0.65	8.89	5.00	131.
0.04	0.638	0.00874	1.40	0.70	10.6	5.65	235.
0.05	0.727	0.0138	1.53	0.75	12.7	6.41	445.
0.06	0.813	0.0203	1.64	0.80	15.6	7.33	911.
0.07	0.896	0.0284	1.75	0.85	19.9	8.55	2.11e+003
0.08	0.978	0.0384	1.86	0.90	26.9	10.3	6.08e+003
0.09	1.06	0.0504	1.96	0.91	28.9	10.8	7.86e+003
0.10	1.14	0.0647	2.07	0.92	31.3	11.3	1.04e+004
0.15	1.54	0.180	2.60	0.93	34.1	12.0	1.41e+004
0.20	1.96	0.393	3.21	0.94	37.6	12.7	1.99e+004
0.25	2.41	0.734	4.02	0.95	42.0	13.6	2.94e+004
0.30	2.90	1.21	5.25	0.96	47.9	14.7	4.66e+004
0.35	3.44	1.76	7.30	0.97	56.2	16.2	8.21e+004
0.40	4.05	2.33	10.8	0.98	69.6	18.4	1.74e+005
0.45	4.74	2.86	16.9	0.99	97.4	22.5	5.72e+005
0.50	5.53	3.38	27.1				

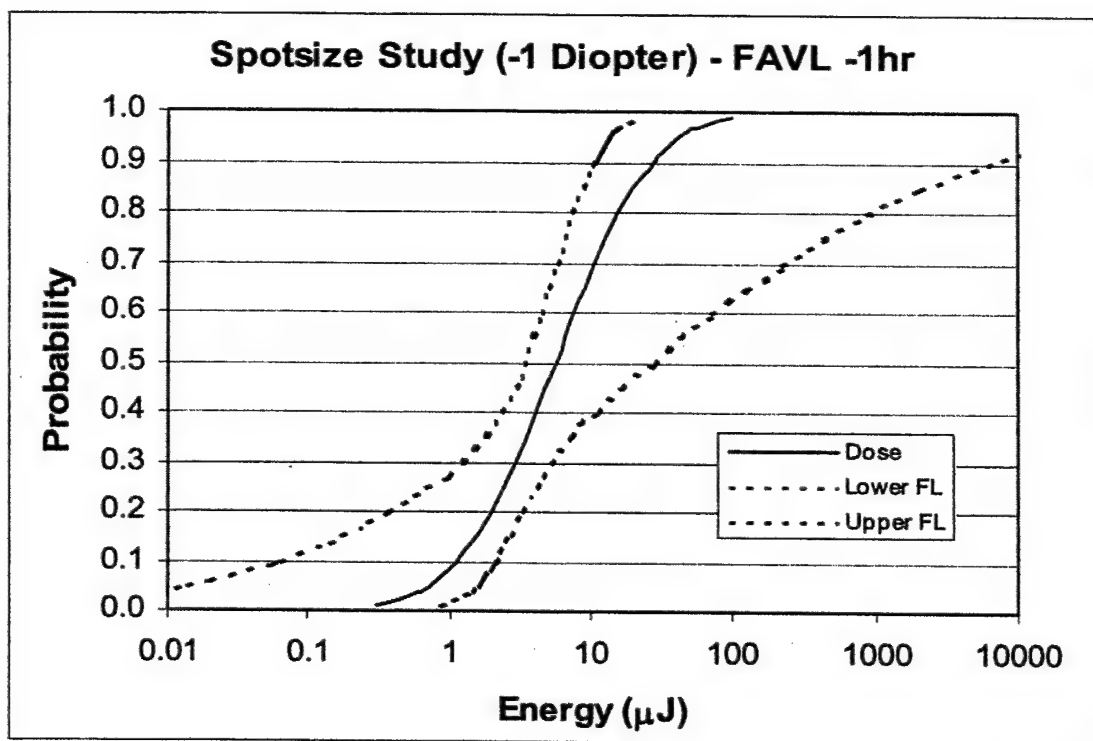
Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0100	1	0	2.18	1	0	4.19	1	0
0.340	1	0	2.25	1	0	4.48	1	0
0.350	2	0	2.40	1	0	4.63	1	0
0.520	1	0	2.49	1	0	4.72	1	0
0.540	1	0	2.66	1	0	4.88	1	1

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.760	1	0	3.13	1	0	4.90	1	0
0.960	2	0	3.18	1	0	5.15	1	1
0.970	1	0	3.20	1	0	5.17	2	1
1.02	1	1	3.25	1	0	5.71	1	1
1.16	1	0	3.26	1	1	6.30	1	1
1.34	1	0	3.29	1	1	6.50	1	0
1.45	1	0	3.37	1	0	6.80	1	0
1.63	1	1	3.75	1	1	7.30	1	1
1.70	1	0	3.76	1	0	11.8	1	1
1.76	1	0	3.78	1	0	24.6	1	1
2.00	1	1	4.13	1	1			

Totals

50

15



**Spotsize Study (-1 Diopter) - FAVL -24hr**  
**A39 OS, C63 OD**

ONES = 4                      ZEROES = 46                      TOTAL = 50

Percent confidence = 0.95

ED50 = 7.36    Upper FL = 4.43e+12                      Lower FL = 5.92

Intercept = -7.91                      Slope = 9.13

Pearson's Chi-Sq = 14.8235    Probability of Chi-Sq = 1.0000

h = 1.00                      g = 0.98                      t = 1.96

Log XBAR = 0.766    Log YBAR = 4.09

SYX = 18.731    SXY = 0.428    SXX = 0.047    S0 = 5.173

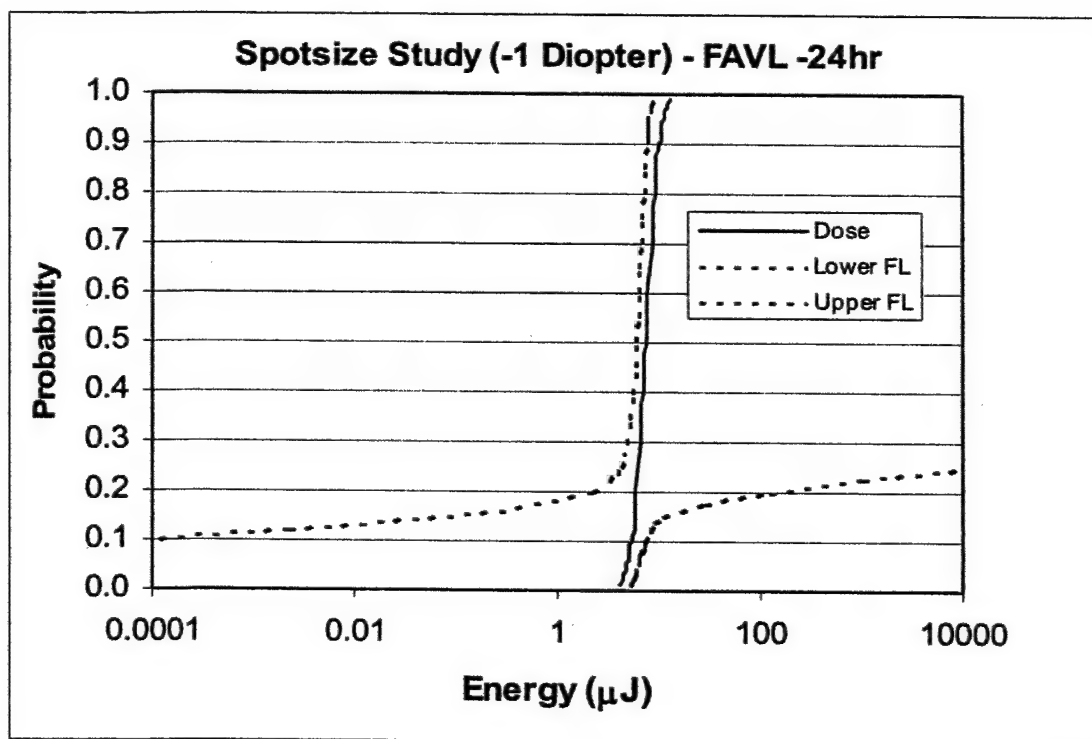
<u>Prob</u>	<u>Dose</u>	<u>LFL</u>	<u>UFL</u>	<u>Prob</u>	<u>Dose</u>	<u>LFL</u>	<u>UFL</u>
0.01	4.09	2.90e-018	5.22	0.55	7.59	6.09	1.85e+014
0.02	4.38	9.64e-015	5.49	0.60	7.84	6.25	8.24e+015
0.03	4.58	1.64e-012	5.70	0.65	8.11	6.40	4.17e+017
0.04	4.73	7.83e-011	5.88	0.70	8.40	6.56	2.61e+019
0.05	4.86	1.80e-009	6.06	0.75	8.72	6.73	2.28e+021
0.06	4.97	2.60e-008	6.23	0.80	9.10	6.91	3.30e+023
0.07	5.07	2.68e-007	6.43	0.85	9.55	7.12	1.09e+026
0.08	5.16	2.15e-006	6.64	0.90	10.2	7.39	1.61e+029
0.09	5.25	1.42e-005	6.88	0.91	10.3	7.45	9.40e+029
0.10	5.32	8.04e-005	7.17	0.92	10.5	7.52	6.39e+030
0.15	5.66	0.0799	11.1	0.93	10.7	7.60	5.25e+031
0.20	5.95	2.37	127.	0.94	10.9	7.69	5.52e+032
0.25	6.21	4.14	1.08e+004	0.95	11.1	7.78	8.07e+033
0.30	6.44	4.84	8.27e+005	0.96	11.4	7.90	1.89e+035
0.35	6.67	5.23	4.91e+007	0.97	11.8	8.05	9.11e+036
0.40	6.90	5.51	2.42e+009	0.98	12.3	8.24	1.57e+039
0.45	7.13	5.73	1.06e+011	0.99	13.2	8.55	5.30e+042
0.50	7.36	5.92	4.43e+012				

<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>
0.0100	1	0	2.18	1	0	4.19	1	0
0.340	1	0	2.25	1	0	4.48	1	0
0.350	2	0	2.40	1	0	4.63	1	0
0.520	1	0	2.49	1	0	4.72	1	0
0.540	1	0	2.66	1	0	4.88	1	0

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.760	1	0	3.13	1	0	4.90	1	0
0.960	2	0	3.18	1	0	5.15	1	1
0.970	1	0	3.20	1	0	5.17	2	0
1.02	1	0	3.25	1	0	5.71	1	0
1.16	1	0	3.26	1	0	6.30	1	0
1.34	1	0	3.29	1	0	6.50	1	0
1.45	1	0	3.37	1	0	6.80	1	0
1.63	1	0	3.75	1	0	7.30	1	1
1.70	1	0	3.76	1	0	11.8	1	1
1.76	1	0	3.78	1	0	24.6	1	1
2.00	1	0	4.13	1	0			

**Totals**

**50 4**





**Spotsize Study (-5 Diopter) - MVL -1hr**  
C91 OS, C17 OD

ONES = 14                      ZEROES = 34                      TOTAL = 48

Percent confidence = 0.95

ED50 = 16.6    Upper FL = 170.                      Lower FL = 9.31

Intercept = -1.96                      Slope = 1.60

Pearson's Chi-Sq = 55.5182    Probability of Chi-Sq = 0.1353

h = 1.00                      g = 0.57                      t = 1.96

Log XBAR = 0.934                      Log YBAR = 4.54

SYX = 62.264    SXY = 4.208    SXX = 2.625    S0 = 23.854

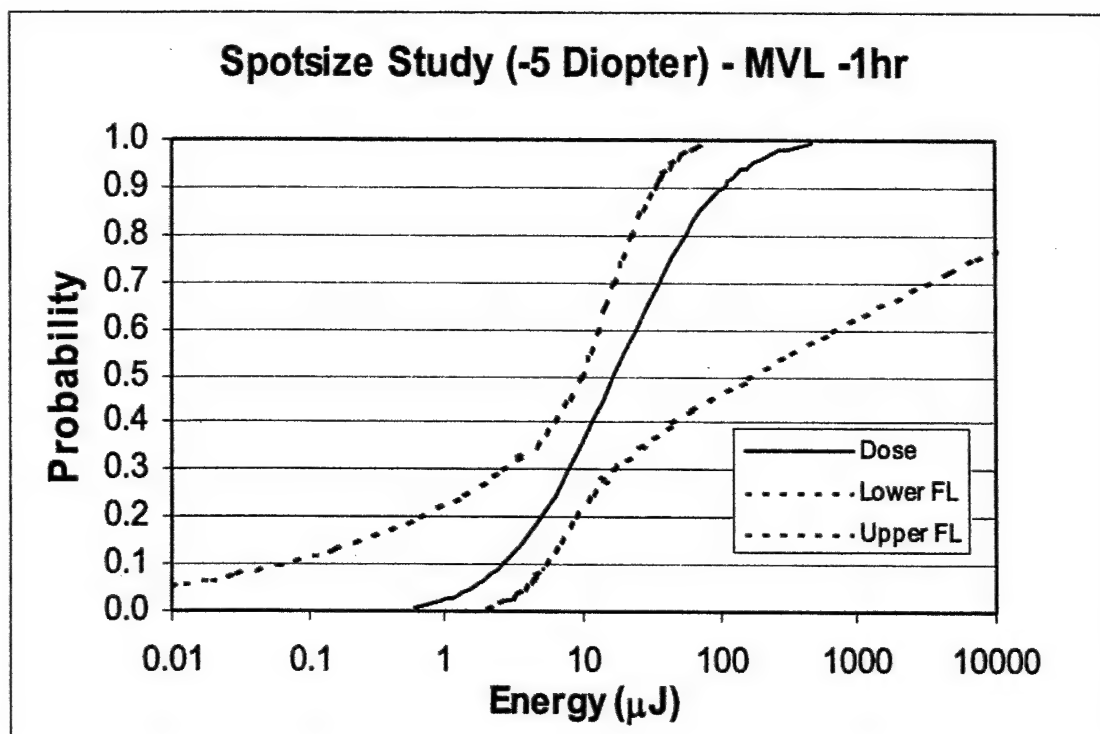
<u>Prob</u>	<u>Dose</u>	<u>LFL</u>	<u>UFL</u>	<u>Prob</u>	<u>Dose</u>	<u>LFL</u>	<u>UFL</u>
0.01	0.588	0.000142	2.02	0.55	19.9	10.9	336.
0.02	0.870	0.000691	2.56	0.60	23.9	12.6	682.
0.03	1.12	0.00188	2.99	0.65	28.9	14.4	1.43e+003
0.04	1.34	0.00399	3.36	0.70	35.3	16.5	3.16e+003
0.05	1.57	0.00733	3.70	0.75	43.8	19.0	7.47e+003
0.06	1.78	0.0123	4.02	0.80	55.7	22.2	1.95e+004
0.07	2.00	0.0193	4.33	0.85	73.6	26.4	6.02e+004
0.08	2.21	0.0289	4.64	0.90	105.	32.7	2.49e+005
0.09	2.42	0.0417	4.94	0.91	114.	34.5	3.51e+005
0.10	2.64	0.0584	5.24	0.92	125.	36.4	5.11e+005
0.15	3.75	0.229	6.84	0.93	138.	38.7	7.70e+005
0.20	4.96	0.652	8.83	0.94	155.	41.4	1.22e+006
0.25	6.31	1.49	11.8	0.95	176.	44.7	2.06e+006
0.30	7.83	2.83	16.9	0.96	205.	49.0	3.81e+006
0.35	9.56	4.48	27.0	0.97	248.	54.7	8.13e+006
0.40	11.5	6.16	47.3	0.98	317.	63.3	2.23e+007
0.45	13.9	7.76	88.1	0.99	469.	79.5	1.09e+008
0.50	16.6	9.31	170.				

<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>
0.0100	1	0	4.43	1	0	9.40	1	0
0.750	1	0	4.61	1	0	9.86	1	0
1.33	1	0	5.69	1	0	10.0	1	0
1.64	1	1	6.00	1	0	12.1	1	1
1.73	1	0	6.59	1	0	12.4	1	0

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
1.91	1	0	6.77	1	0	14.5	2	1
2.22	1	1	6.80	1	0	17.0	1	0
3.21	1	0	7.60	1	1	19.4	1	0
3.31	1	0	7.71	1	0	19.6	1	1
3.38	1	0	7.88	1	0	20.8	1	1
3.49	1	0	8.00	1	0	25.2	1	1
3.57	1	0	8.17	1	0	25.9	1	1
3.60	1	0	8.42	1	0	28.8	1	1
3.89	1	0	8.68	1	0	32.9	1	1
4.10	1	0	8.78	1	0	36.1	1	1
4.22	1	1	9.11	1	1			

Totals

48 14



**Spotsize Study (-5 Diopter) - MVL -24hr**  
**C91 OS, C17 OD**

ONES =23                      ZEROES = 25                      TOTAL = 48

Percent confidence = 0.95

ED50 = 7.18    Upper FL = 9.94            Lower FL = 5.19

Intercept = -3.24            Slope = 3.79

Pearson's Chi-Sq = 35.2495    Probability of Chi-Sq = 0.8512

h = 1.00            g = 0.27            t = 1.96

Log XBAR = 0.856                      Log YBAR = 5.00

SY Y = 49.289 SXY = 3.708    SXX = 0.979    S0 = 18.512

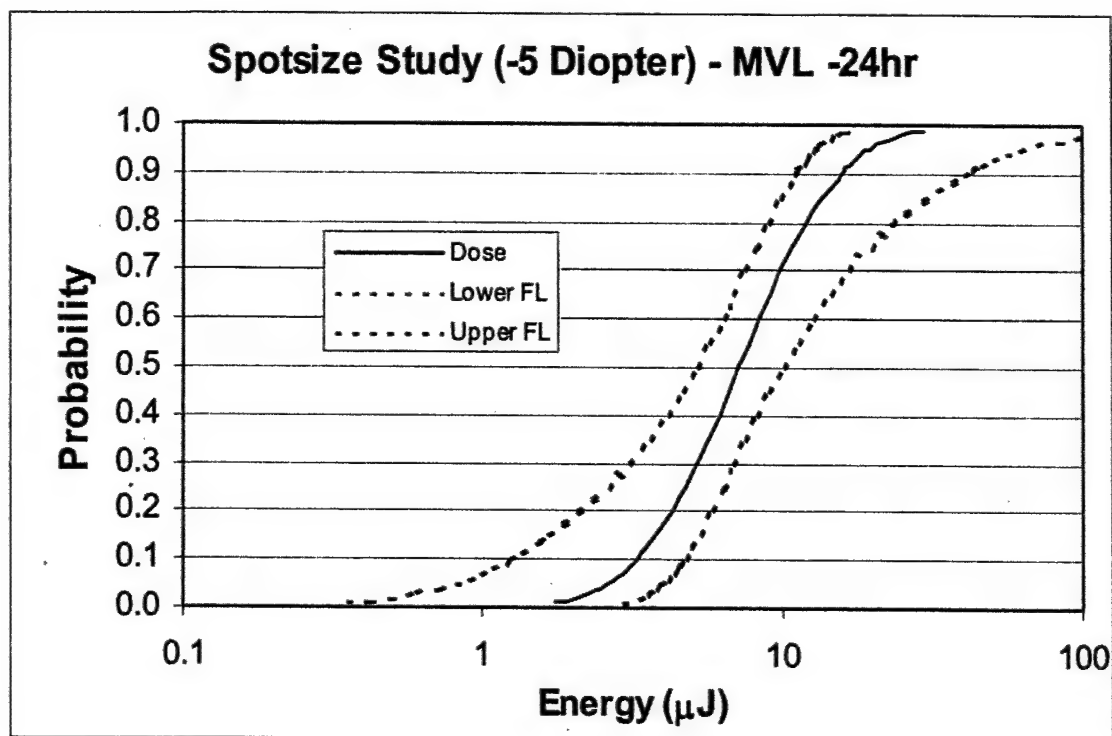
Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	1.75	0.351	2.98	0.55	7.75	5.74	11.1
0.02	2.06	0.494	3.35	0.60	8.38	6.30	12.5
0.03	2.29	0.613	3.61	0.65	9.08	6.88	14.3
0.04	2.48	0.721	3.81	0.70	9.88	7.48	16.6
0.05	2.64	0.822	3.99	0.75	10.8	8.14	19.6
0.06	2.79	0.919	4.16	0.80	12.0	8.89	23.7
0.07	2.93	1.01	4.30	0.85	13.5	9.79	29.9
0.08	3.06	1.10	4.44	0.90	15.7	11.0	40.1
0.09	3.18	1.19	4.57	0.91	16.2	11.3	43.2
0.10	3.29	1.28	4.70	0.92	16.9	11.6	46.7
0.15	3.82	1.72	5.27	0.93	17.6	12.0	50.9
0.20	4.31	2.17	5.80	0.94	18.5	12.4	56.1
0.25	4.77	2.63	6.34	0.95	19.5	12.9	62.7
0.30	5.22	3.11	6.89	0.96	20.8	13.5	71.5
0.35	5.68	3.61	7.50	0.97	22.5	14.3	84.0
0.40	6.16	4.12	8.19	0.98	25.0	15.4	104.
0.45	6.65	4.65	8.99	0.99	29.6	17.3	147.
0.50	7.18	5.19	9.94				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0100	1	0	4.43	1	1	9.40	1	1
0.750	1	0	4.61	1	0	9.86	1	0
1.33	1	0	5.69	1	1	10.0	1	1
1.64	1	0	6.00	1	0	12.1	1	1
1.73	1	0	6.59	1	0	12.4	1	1

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
1.91	1	0	6.77	1	0	14.5	2	2
2.22	1	0	6.80	1	0	17.0	1	1
3.21	1	0	7.60	1	1	19.4	1	1
3.31	1	0	7.71	1	0	19.6	1	1
3.38	1	0	7.88	1	1	20.8	1	1
3.49	1	0	8.00	1	0	25.2	1	1
3.57	1	0	8.17	1	0	25.9	1	1
3.60	1	1	8.42	1	0	28.8	1	1
3.89	1	0	8.68	1	0	32.9	1	1
4.10	1	0	8.78	1	1	36.1	1	1
4.22	1	1	9.11	1	1			

Totals

48 23



**Spotsize Study (-5 Diopter) -FAVL 1hr**  
**C91 OS, C17 OD**

ONES = 16                      ZEROES = 32                      TOTAL = 48

Percent confidence = 0.95

ED50 = 10.1    Upper FL = 14.1                      Lower FL = 8.36

Intercept = -8.01                      Slope = 7.97

Pearson's Chi-Sq = 19.9360    Probability of Chi-Sq = 0.9996

h = 1.00                      g = 0.44                      t = 1.96

Log XBAR = 0.966    Log YBAR = 4.69

SYX = 28.646    SXY = 1.093    SXX = 0.137    S0 = 10.098

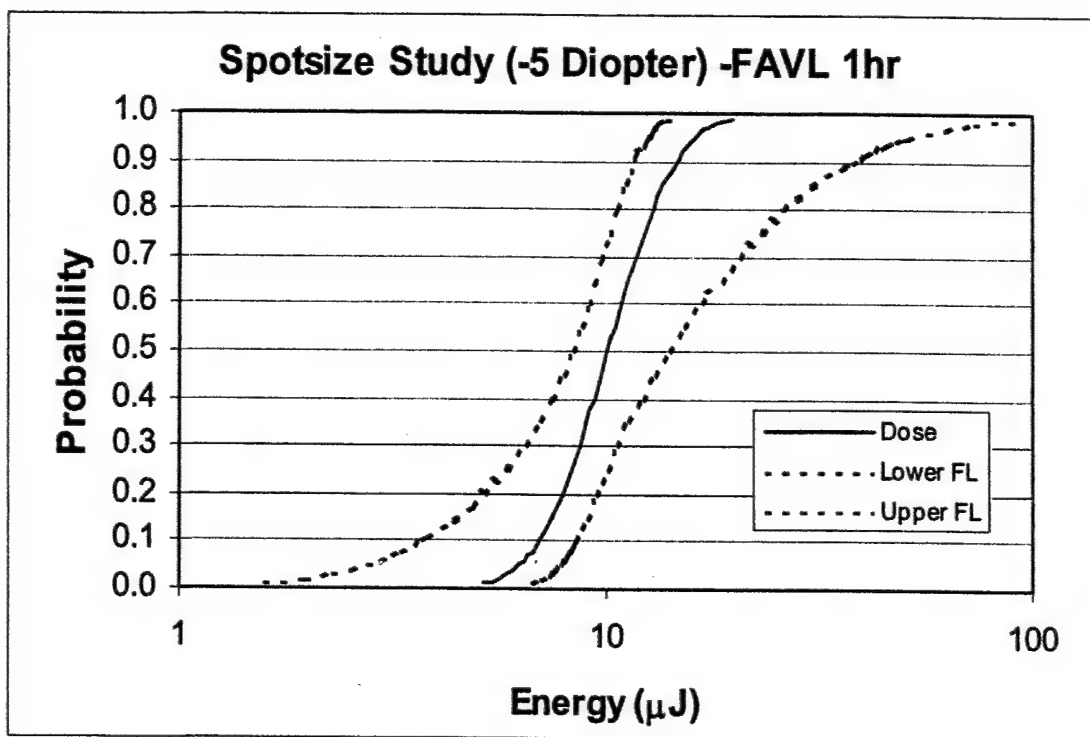
Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	5.17	1.57	6.79	0.55	10.5	8.75	15.3
0.02	5.59	1.97	7.16	0.60	10.9	9.11	16.8
0.03	5.88	2.28	7.41	0.65	11.3	9.46	18.6
0.04	6.10	2.54	7.61	0.70	11.8	9.81	20.7
0.05	6.29	2.77	7.78	0.75	12.3	10.2	23.3
0.06	6.46	2.98	7.93	0.80	12.9	10.6	26.6
0.07	6.61	3.18	8.07	0.85	13.7	11.0	31.2
0.08	6.74	3.36	8.20	0.90	14.7	11.6	38.2
0.09	6.87	3.54	8.32	0.91	14.9	11.7	40.1
0.10	6.99	3.71	8.44	0.92	15.2	11.9	42.3
0.15	7.50	4.50	8.97	0.93	15.5	12.1	44.9
0.20	7.94	5.20	9.49	0.94	15.9	12.3	48.0
0.25	8.33	5.85	10.0	0.95	16.3	12.5	51.7
0.30	8.70	6.45	10.6	0.96	16.8	12.7	56.6
0.35	9.05	7.00	11.3	0.97	17.4	13.0	63.1
0.40	9.40	7.50	12.1	0.98	18.3	13.5	73.0
0.45	9.76	7.95	13.0	0.99	19.8	14.2	92.0
0.50	10.1	8.36	14.1				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0100	1	0	4.43	1	0	9.40	1	0
0.750	1	0	4.61	1	0	9.86	1	0
1.33	1	0	5.69	1	0	10.0	1	1
1.64	1	0	6.00	1	0	12.1	1	1
1.73	1	0	6.59	1	0	12.4	1	0

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
1.91	1	0	6.77	1	0	14.5	2	2
2.22	1	0	6.80	1	0	17.0	1	1
3.21	1	0	7.60	1	1	19.4	1	1
3.31	1	0	7.71	1	0	19.6	1	1
3.38	1	0	7.88	1	1	20.8	1	1
3.49	1	0	8.00	1	0	25.2	1	1
3.57	1	0	8.17	1	0	25.9	1	1
3.60	1	0	8.42	1	0	28.8	1	1
3.89	1	0	8.68	1	0	32.9	1	1
4.10	1	0	8.78	1	0	36.1	1	1
4.22	1	0	9.11	1	1			

Totals

48 16



**Spotsize Study (-5 Diopter) -FAVL -24hr**  
**C91 OS, C17 OD**

ONES = 13                      ZEROES = 35                      TOTAL = 48

Percent confidence = 0.95

ED50 = 12.1    Upper FL = 17.3                      Lower FL = 9.72

Intercept = -7.07                      Slope = 6.52

Pearson's Chi-Sq = 23.3188    Probability of Chi-Sq = 0.9969

h = 1.00                      g = 0.34                      t = 1.96

Log XBAR = 1.03                      Log YBAR = 4.64

SYX = 34.651    SXY = 1.738    SXX = 0.267    S0 = 10.395

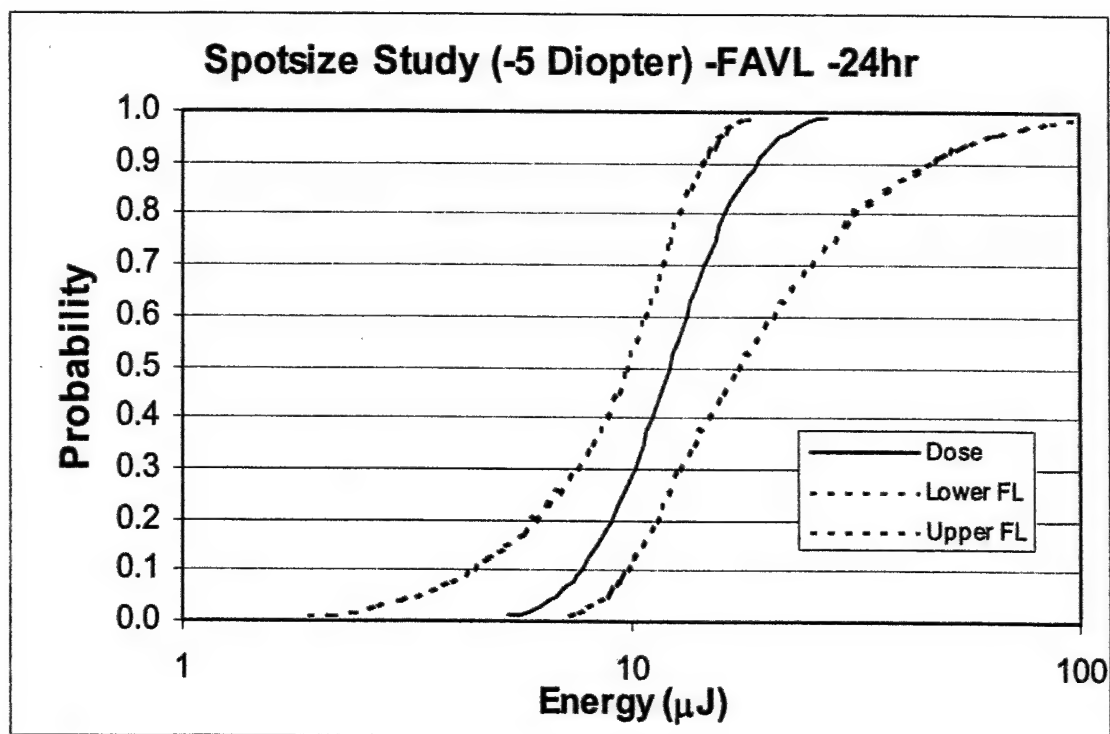
Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	5.33	1.92	7.27	0.55	12.7	10.2	18.8
0.02	5.87	2.40	7.79	0.60	13.3	10.7	20.6
0.03	6.24	2.76	8.14	0.65	13.9	11.2	22.6
0.04	6.53	3.07	8.43	0.70	14.6	11.7	25.1
0.05	6.78	3.34	8.68	0.75	15.4	12.2	28.2
0.06	7.00	3.58	8.89	0.80	16.3	12.8	32.1
0.07	7.20	3.81	9.10	0.85	17.5	13.5	37.5
0.08	7.38	4.03	9.29	0.90	19.1	14.4	45.7
0.09	7.55	4.23	9.46	0.91	19.5	14.7	48.0
0.10	7.71	4.43	9.64	0.92	19.9	14.9	50.5
0.15	8.41	5.32	10.4	0.93	20.4	15.2	53.5
0.20	9.01	6.10	11.2	0.94	21.0	15.5	57.1
0.25	9.56	6.82	12.0	0.95	21.7	15.8	61.5
0.30	10.1	7.48	12.8	0.96	22.5	16.2	67.1
0.35	10.6	8.10	13.7	0.97	23.6	16.8	74.7
0.40	11.1	8.67	14.8	0.98	25.0	17.5	86.1
0.45	11.6	9.21	15.9	0.99	27.6	18.7	108.
0.50	12.1	9.72	17.3				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0100	1	0	4.43	1	0	9.40	1	0
0.750	1	0	4.61	1	0	9.86	1	0
1.33	1	0	5.69	1	0	10.0	1	0
1.64	1	0	6.00	1	0	12.1	1	1
1.73	1	0	6.59	1	0	12.4	1	0

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
1.91	1	0	6.77	1	0	14.5	2	1
2.22	1	0	6.80	1	0	17.0	1	1
3.21	1	0	7.60	1	1	19.4	1	1
3.31	1	0	7.71	1	0	19.6	1	1
3.38	1	0	7.88	1	1	20.8	1	1
3.49	1	0	8.00	1	0	25.2	1	1
3.57	1	0	8.17	1	0	25.9	1	1
3.60	1	0	8.42	1	0	28.8	1	1
3.89	1	0	8.68	1	0	32.9	1	1
4.10	1	0	8.78	1	0	36.1	1	1
4.22	1	0	9.11	1	0			

Totals

48 13





**Spotsize Study (-10 Diopter) - MVL - 1hr**  
**C91 OD, B99 OS**

ONES = 12                  ZEROES = 31                  TOTAL = 43

Percent confidence = 0.95

ED50 = 38.1    Upper FL = 72.1                  Lower FL = 28.2

Intercept = -5.87                  Slope = 3.71

Pearson's Chi-Sq = 28.8479    Probability of Chi-Sq = 0.8286

h = 1.00                  g = 0.41                  t = 1.96

Log XBAR = 1.48                  Log YBAR = 4.61

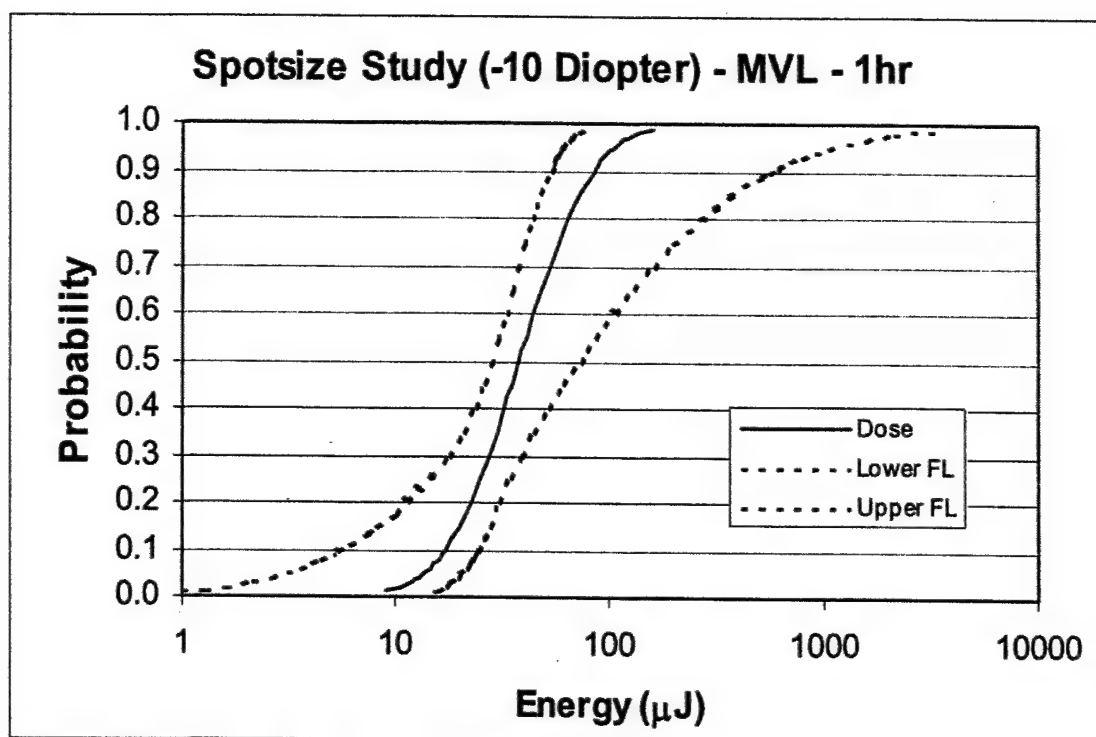
SY Y = 38.204 SXY = 2.520    SXX = 0.679    S0 = 16.603

<u>Prob</u>	<u>Dose</u>	<u>LFL</u>	<u>UFL</u>	<u>Prob</u>	<u>Dose</u>	<u>LFL</u>	<u>UFL</u>
0.01	9.01	0.999	15.2	0.55	41.2	30.6	86.7
0.02	10.7	1.59	17.0	0.60	44.6	32.9	105.
0.03	11.9	2.12	18.3	0.65	48.4	35.3	130.
0.04	12.9	2.64	19.4	0.70	52.8	37.8	162.
0.05	13.8	3.15	20.3	0.75	57.9	40.6	207.
0.06	14.5	3.66	21.1	0.80	64.3	43.7	273.
0.07	15.3	4.17	21.9	0.85	72.5	47.6	378.
0.08	16.0	4.68	22.6	0.90	84.4	52.8	572.
0.09	16.6	5.20	23.3	0.91	87.6	54.1	632.
0.10	17.2	5.72	24.0	0.92	91.1	55.5	704.
0.15	20.1	8.45	27.2	0.93	95.2	57.2	794.
0.20	22.6	11.4	30.5	0.94	100.	59.0	908.
0.25	25.1	14.4	34.2	0.95	106.	61.2	1.06e+003
0.30	27.5	17.4	38.7	0.96	113.	63.9	1.27e+003
0.35	30.0	20.4	44.4	0.97	122.	67.3	1.58e+003
0.40	32.6	23.2	51.5	0.98	136.	72.1	2.12e+003
0.45	35.3	25.8	60.6	0.99	161.	80.3	3.39e+003
0.50	38.1	28.2	72.1				

<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>
6.10	1	0	17.9	1	0	33.8	1	0
6.70	1	0	18.5	1	1	34.2	1	0
7.07	1	0	18.9	1	0	36.3	1	0
7.30	2	0	20.2	1	0	37.4	1	1
9.10	1	0	20.9	1	0	38.3	1	1

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
9.40	1	0	21.8	1	0	42.2	1	1
10.3	1	0	21.9	1	0	43.6	1	1
10.5	1	0	22.6	1	0	44.1	2	2
11.1	1	0	24.0	1	0	47.2	1	1
11.4	1	0	25.2	1	0	49.4	2	1
12.4	1	0	27.2	1	0	49.6	1	0
14.2	2	1	29.0	1	0	64.8	1	1
14.8	1	0	33.0	1	0	194.	1	1

Totals 43 12



**Spotsize Study (-10 Diopter) - MVL - 24hr**  
**C91 OD, B99 OS**

ONES = 24                      ZEROES = 19                      TOTAL = 43

Percent confidence = 0.95

ED50 = 19.7    Upper FL = 25.3                      Lower FL = 14.7

Intercept = -6.43                      Slope = 4.97

Pearson's Chi-Sq = 28.8935    Probability of Chi-Sq = 0.8270

h = 1.00                      g = 0.25                      t = 1.96

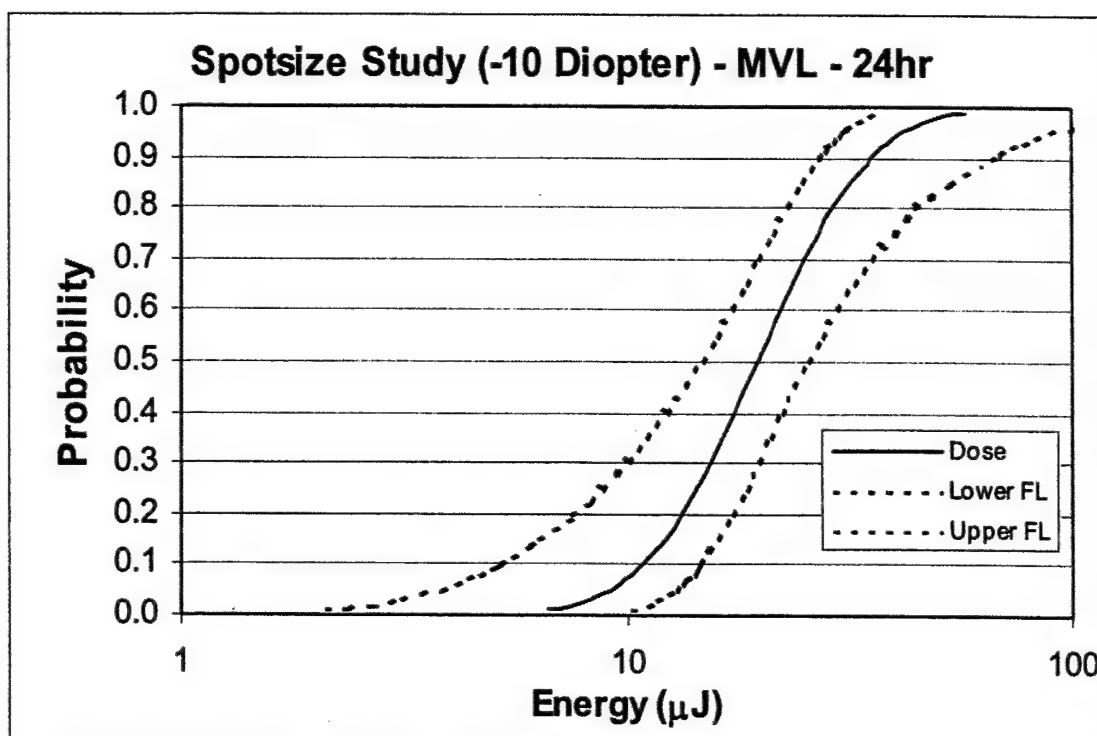
Log XBAR = 1.32                      Log YBAR = 5.13

SY Y = 44.517 SXY = 3.143    SXX = 0.632    S0 = 14.995

<u>Prob</u>	<u>Dose</u>	<u>LFL</u>	<u>UFL</u>	<u>Prob</u>	<u>Dose</u>	<u>LFL</u>	<u>UFL</u>
0.01	6.70	2.09	10.2	0.55	20.9	15.9	27.3
0.02	7.60	2.67	11.2	0.60	22.1	17.2	29.6
0.03	8.23	3.11	11.9	0.65	23.5	18.5	32.4
0.04	8.74	3.49	12.4	0.70	25.1	19.8	35.8
0.05	9.18	3.84	12.9	0.75	26.9	21.3	40.1
0.06	9.57	4.16	13.3	0.80	29.1	22.9	45.7
0.07	9.93	4.46	13.6	0.85	31.8	24.8	53.7
0.08	10.3	4.74	14.0	0.90	35.6	27.2	66.0
0.09	10.6	5.02	14.3	0.91	36.6	27.8	69.4
0.10	10.9	5.29	14.6	0.92	37.7	28.5	73.4
0.15	12.2	6.53	15.9	0.93	39.0	29.2	78.0
0.20	13.3	7.71	17.2	0.94	40.4	30.1	83.6
0.25	14.4	8.85	18.4	0.95	42.1	31.0	90.4
0.30	15.4	10.0	19.6	0.96	44.3	32.2	99.3
0.35	16.5	11.1	20.8	0.97	47.0	33.7	111.
0.40	17.5	12.3	22.2	0.98	50.9	35.7	130.
0.45	18.6	13.5	23.7	0.99	57.8	39.1	166.
0.50	19.7	14.7	25.3				

<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>
6.10	1	0	17.9	1	0	33.8	1	0
6.70	1	0	18.5	1	1	34.2	1	1
7.07	1	0	18.9	1	1	36.3	1	1
7.30	2	0	20.2	1	1	37.4	1	1
9.10	1	0	20.9	1	0	38.3	1	1

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
9.40	1	0	21.8	1	1	42.2	1	1
10.3	1	0	21.9	1	1	43.6	1	1
10.5	1	0	22.6	1	1	44.1	2	2
11.1	1	0	24.0	1	1	47.2	1	1
11.4	1	0	25.2	1	1	49.4	2	2
12.4	1	0	27.2	1	1	49.6	1	1
14.2	2	1	29.0	1	0	64.8	1	1
14.8	1	0	33.0	1	0	194.	1	1
<b>Totals</b>							<b>43</b>	<b>24</b>



**Spotsize Study (-10 Diopter) - FAVL - 1hr**  
**C91 OD, B99 OS**

ONES = 14                  ZEROES = 29                  TOTAL = 43

Percent confidence = 0.95

ED50 = 32.1    Upper FL = 40.8                  Lower FL = 25.6

Intercept = -10.4                  Slope = 6.90

Pearson's Chi-Sq = 31.4620    Probability of Chi-Sq = 0.7259

h = 1.00                  g = 0.33                  t = 1.96

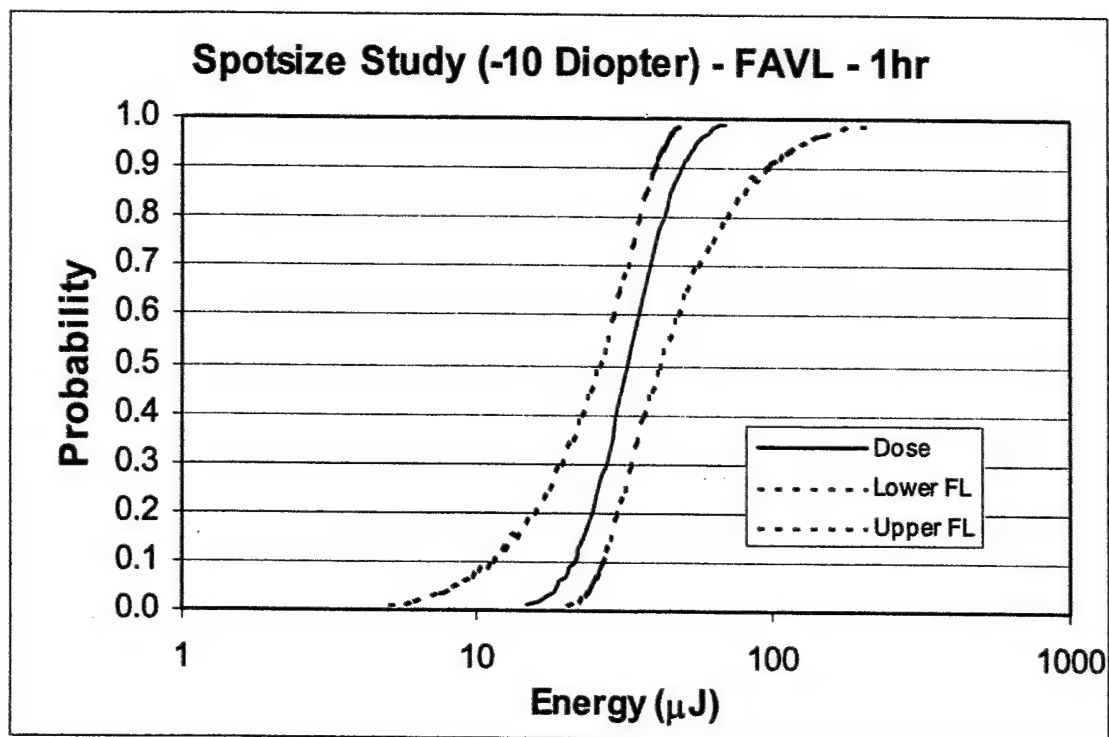
Log XBAR = 1.50                  Log YBAR = 4.96

SY Y = 42.975 SXY = 1.669    SXX = 0.242    S0 = 11.985

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	14.8	5.00	20.3	0.55	33.5	27.2	43.6
0.02	16.2	6.17	21.7	0.60	35.0	28.7	46.9
0.03	17.2	7.04	22.5	0.65	36.5	30.2	50.9
0.04	17.9	7.78	23.3	0.70	38.3	31.7	55.8
0.05	18.6	8.43	23.9	0.75	40.2	33.3	61.8
0.06	19.1	9.03	24.4	0.80	42.6	35.0	69.5
0.07	19.6	9.58	24.9	0.85	45.4	36.9	80.0
0.08	20.1	10.1	25.3	0.90	49.3	39.3	96.0
0.09	20.5	10.6	25.7	0.91	50.3	39.9	100.
0.10	21.0	11.1	26.1	0.92	51.4	40.6	105.
0.15	22.7	13.3	27.9	0.93	52.6	41.3	111.
0.20	24.3	15.3	29.5	0.94	54.0	42.1	118.
0.25	25.7	17.1	31.0	0.95	55.6	43.0	126.
0.30	27.0	19.0	32.6	0.96	57.6	44.1	137.
0.35	28.3	20.7	34.3	0.97	60.2	45.5	151.
0.40	29.5	22.4	36.2	0.98	63.8	47.3	173.
0.45	30.8	24.0	38.3	0.99	69.9	50.4	213.
0.50	32.1	25.6	40.8				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
6.10	1	0	17.9	1	0	33.8	1	0
6.70	1	0	18.5	1	0	34.2	1	0
7.07	1	0	18.9	1	1	36.3	1	1
7.30	2	0	20.2	1	0	37.4	1	0
9.10	1	0	20.9	1	0	38.3	1	1

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
9.40	1	0	21.8	1	0	42.2	1	1
10.3	1	0	21.9	1	0	43.6	1	1
10.5	1	0	22.6	1	0	44.1	2	2
11.1	1	0	24.0	1	1	47.2	1	1
11.4	1	0	25.2	1	0	49.4	2	2
12.4	1	0	27.2	1	0	49.6	1	1
14.2	2	0	29.0	1	0	64.8	1	1
14.8	1	0	33.0	1	0	194.	1	1
<b>Totals</b>							<b>43</b>	<b>14</b>



**Spotsize Study (-10 Diopter) - FAVL - 24hr**  
**C91 OD, B99 OS**

ONES = 13                      ZEROES = 30                      TOTAL = 43

Percent confidence = 0.95

ED50 = 35.3    Upper FL = 57.8                      Lower FL = 26.6

Intercept = -6.27                      Slope = 4.05

Pearson's Chi-Sq = 31.5524    Probability of Chi-Sq = 0.7220

h = 1.00                      g = 0.38                      t = 1.96

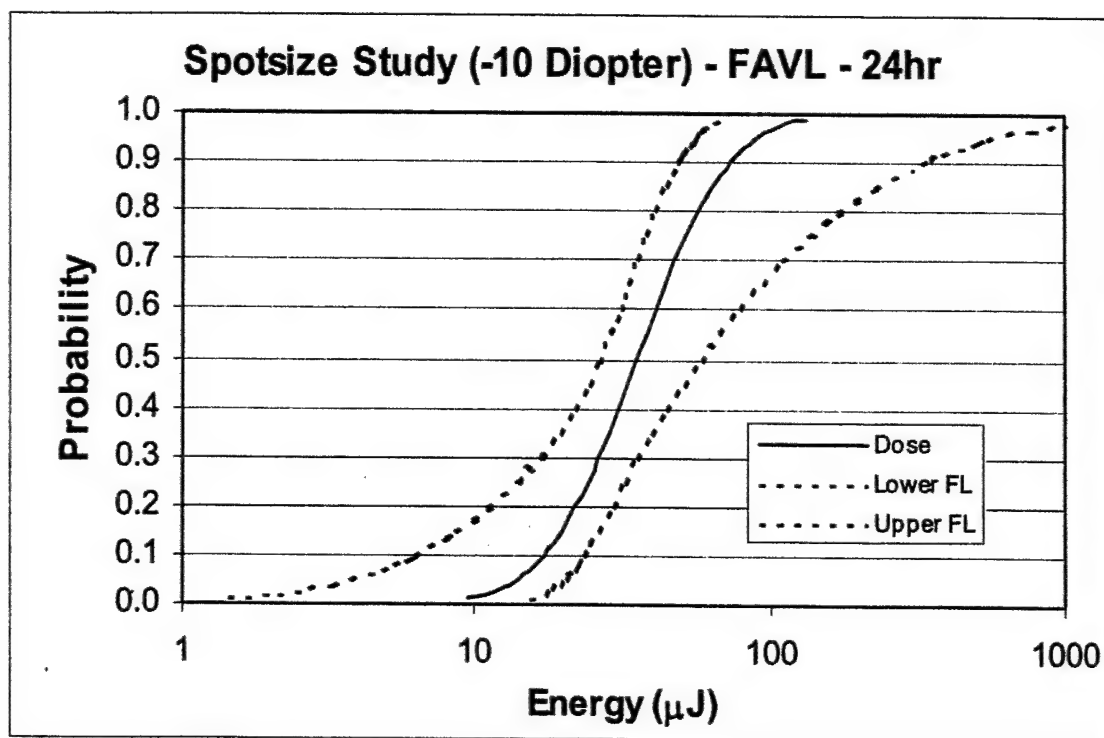
Log XBAR = 1.47                      Log YBAR = 4.70

SY Y = 41.730 SXY = 2.513    SXX = 0.621    S0 = 16.373

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	9.42	1.43	15.4	0.55	38.0	28.8	67.2
0.02	11.0	2.12	17.1	0.60	40.8	31.0	79.0
0.03	12.1	2.72	18.2	0.65	44.0	33.1	93.9
0.04	13.1	3.27	19.2	0.70	47.6	35.4	113.
0.05	13.9	3.81	20.0	0.75	51.9	37.9	139.
0.06	14.6	4.33	20.8	0.80	57.0	40.7	176.
0.07	15.3	4.84	21.5	0.85	63.7	44.1	231.
0.08	15.9	5.34	22.1	0.90	73.2	48.7	329.
0.09	16.5	5.85	22.7	0.91	75.7	49.8	358.
0.10	17.1	6.35	23.3	0.92	78.6	51.1	393.
0.15	19.6	8.87	26.1	0.93	81.8	52.5	435.
0.20	21.9	11.5	28.9	0.94	85.5	54.1	487.
0.25	24.1	14.1	31.8	0.95	90.0	56.0	555.
0.30	26.2	16.8	35.2	0.96	95.6	58.2	647.
0.35	28.4	19.4	39.2	0.97	103.	61.1	781.
0.40	30.6	21.9	44.2	0.98	114.	65.2	1.00e+003
0.45	32.9	24.3	50.3	0.99	133.	72.1	1.50e+003
0.50	35.3	26.6	57.8				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
6.10	1	0	17.9	1	0	33.8	1	0
6.70	1	0	18.5	1	0	34.2	1	0
7.07	1	0	18.9	1	1	36.3	1	0
7.30	2	0	20.2	1	0	37.4	1	0
9.10	1	0	20.9	1	0	38.3	1	0

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
9.40	1	0	21.8	1	1	42.2	1	1
10.3	1	0	21.9	1	1	43.6	1	0
10.5	1	0	22.6	1	0	44.1	2	2
11.1	1	0	24.0	1	1	47.2	1	1
11.4	1	0	25.2	1	0	49.4	2	2
12.4	1	0	27.2	1	0	49.6	1	1
14.2	2	0	29.0	1	0	64.8	1	1
14.8	1	0	33.0	1	0	194.	1	1
<b>Totals</b>							<b>43</b>	<b>13</b>





**Spotsize Study (+4.5 Diopter) MVL - 1hr**  
**C77 OS, C77 OD, C65 OS**

ONES = 21                      ZEROES = 19                      TOTAL = 40

Percent confidence = 0.95

ED50 = 80.8    Upper FL = 142.                      Lower FL = 40.8

Intercept =        3.97    Slope = 2.08

Pearson's Chi-Sq = 36.6716    Probability of Chi-Sq = 0.4375

h = 1.00            g = 0.36            t = 1.96

Log XBAR = 1.95    Log YBAR = 5.09

SYX = 47.272    SXY = 5.090    SXX = 2.444    S0 = 19.437

<u>Prob</u>	<u>Dose</u>	<u>LFL</u>	<u>UFL</u>	<u>Prob</u>	<u>Dose</u>	<u>LFL</u>	<u>UFL</u>
0.01	6.17	0.100	18.2	0.55	92.8	51.1	175.
0.02	8.34	0.212	22.1	0.60	107.	62.4	224.
0.03	10.1	0.340	25.1	0.65	124.	74.7	295.
0.04	11.7	0.485	27.6	0.70	144.	88.2	405.
0.05	13.1	0.647	29.9	0.75	170.	103.	582.
0.06	14.5	0.827	32.0	0.80	205.	121.	886.
0.07	15.8	1.02	33.9	0.85	254.	144.	1.47e+003
0.08	17.1	1.24	35.8	0.90	333.	176.	2.81e+003
0.09	18.3	1.48	37.6	0.91	356.	184.	3.29e+003
0.10	19.6	1.73	39.3	0.92	382.	194.	3.90e+003
0.15	25.7	3.34	47.8	0.93	413.	205.	4.72e+003
0.20	31.9	5.58	56.1	0.94	450.	218.	5.84e+003
0.25	38.3	8.61	65.0	0.95	498.	233.	7.46e+003
0.30	45.2	12.6	74.8	0.96	559.	253.	9.94e+003
0.35	52.7	17.7	86.3	0.97	646.	278.	1.42e+004
0.40	61.0	24.0	100.	0.98	782.	316.	2.27e+004
0.45	70.3	31.8	118.	0.99	1.06e+003	386.	4.79e+004
0.50	80.8	40.8	142.				

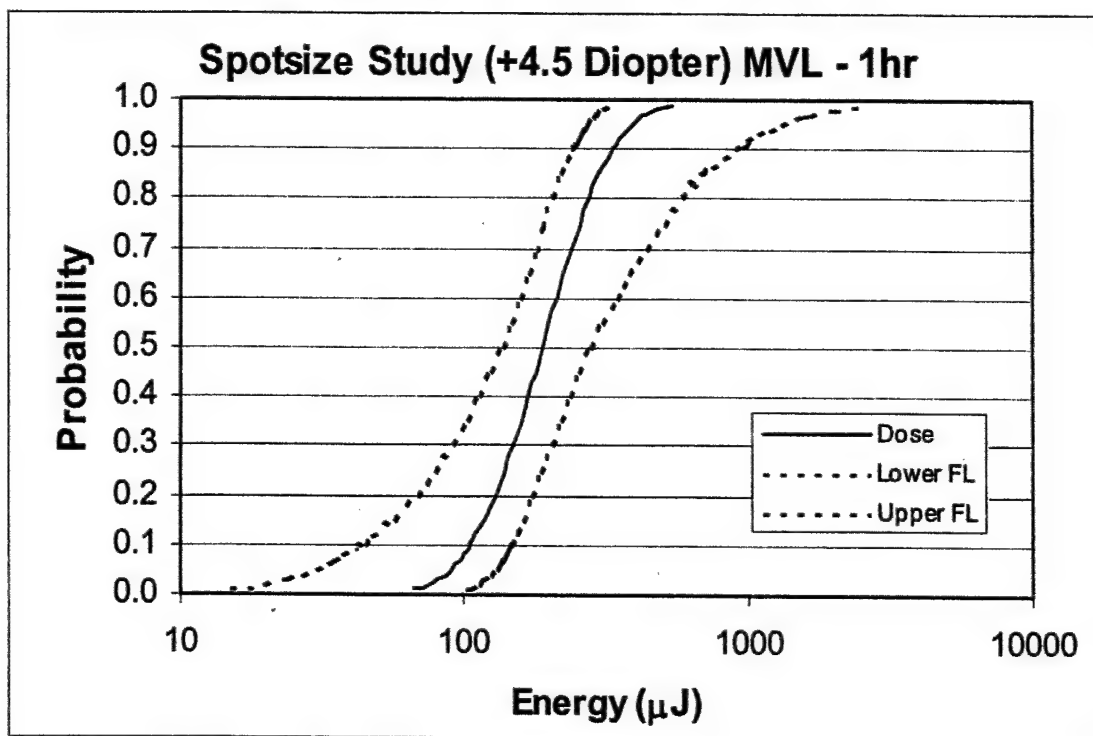
<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>
7.30	1	0	60.0	2	0	180.	1	1
8.00	1	0	61.0	1	1	204.	1	0
12.0	1	0	64.0	1	0	209.	1	1
14.0	1	0	73.0	1	0	232.	1	1
20.0	1	0	80.0	1	1	238.	1	1

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
31.0	1	1	88.0	1	0	283.	1	0
36.0	1	0	91.0	2	2	302.	1	1
37.0	1	0	96.0	1	1	320.	1	1
43.0	1	1	103.	1	1	322.	1	1
45.0	1	0	108.	1	0	394.	1	1
50.0	1	0	118.	1	0	416.	1	1
55.0	1	0	165.	1	1	426.	1	1
57.0	1	1	167.	1	1			

Totals

40

21



**Spotsize Study (+4.5 Diopter) MVL - 24hr**  
**C77 OS, C77 OD, C65 OS**

ONES = 26                      ZEROES = 14                      TOTAL = 40

Percent confidence = 0.95

ED50 = 54.1    Upper FL = 80.1                      Lower FL = 28.0

Intercept = 5.48                      Slope = 3.16

Pearson's Chi-Sq = 24.8523    Probability of Chi-Sq = 0.9192

h = 1.00                      g = 0.37                      t = 1.96

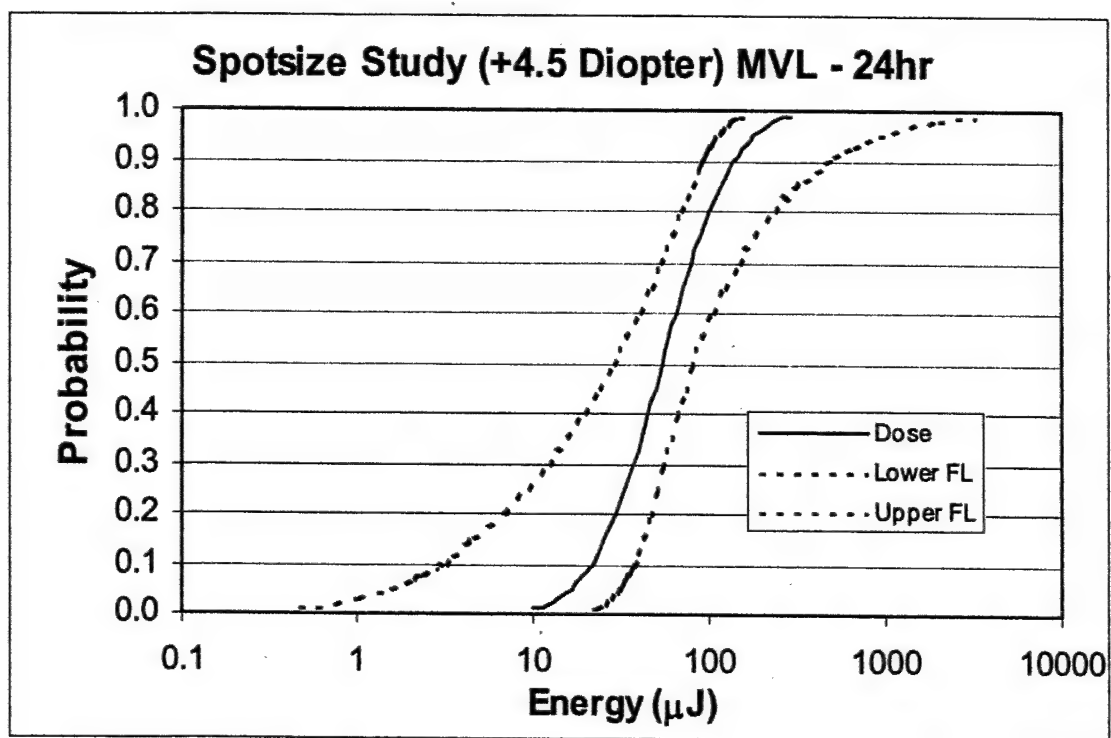
Log XBAR = 1.83                      Log YBAR = 5.31

SY Y = 35.117 SXY = 3.246    SXX = 1.027    S0 = 14.264

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	9.94	0.456	21.9	0.55	59.3	33.4	89.9
0.02	12.1	0.755	24.9	0.60	65.1	39.4	103.
0.03	13.8	1.04	27.1	0.65	71.6	45.8	120.
0.04	15.1	1.32	28.8	0.70	79.3	52.7	144.
0.05	16.3	1.60	30.4	0.75	88.4	60.2	179.
0.06	17.4	1.89	31.7	0.80	99.9	68.4	232.
0.07	18.5	2.19	33.0	0.85	115.	78.1	320.
0.08	19.5	2.49	34.2	0.90	138.	90.6	488.
0.09	20.4	2.80	35.3	0.91	144.	93.7	542.
0.10	21.3	3.12	36.4	0.92	151.	97.2	607.
0.15	25.4	4.86	41.3	0.93	159.	101.	688.
0.20	29.3	6.89	45.8	0.94	168.	105.	792.
0.25	33.1	9.26	50.4	0.95	179.	111.	931.
0.30	36.9	12.0	55.0	0.96	194.	117.	1.13e+003
0.35	40.9	15.2	60.1	0.97	213.	125.	1.43e+003
0.40	45.0	18.9	65.7	0.98	241.	136.	1.96e+003
0.45	49.4	23.2	72.2	0.99	294.	156.	3.23e+003
0.50	54.1	28.0	80.1				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
7.30	1	0	60.0	2	1	180.	1	1
8.00	1	0	61.0	1	1	204.	1	1
12.0	1	0	64.0	1	0	209.	1	1
14.0	1	0	73.0	1	1	232.	1	1
20.0	1	0	80.0	1	1	238.	1	1

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
31.0	1	1	88.0	1	0	283.	1	1
36.0	1	0	91.0	2	2	302.	1	1
37.0	1	1	96.0	1	1	320.	1	1
43.0	1	0	103.	1	1	322.	1	1
45.0	1	0	108.	1	1	394.	1	1
50.0	1	1	118.	1	0	416.	1	1
55.0	1	0	165.	1	1	426.	1	1
57.0	1	0	167.	1	1			
<b>Totals</b>							<b>40</b>	<b>26</b>



**Spotsize Study (+4.5 Diopter) FAVL - 1hr**  
**C77 OS, C77 OD, C65 OS**

ONES = 11                      ZEROES = 29                      TOTAL = 40

Percent confidence = 0.95

ED50 = 189.    Upper FL = 279.            Lower FL = 135.

Intercept = 11.7            Slope = 5.13

Pearson's Chi-Sq = 19.4379    Probability of Chi-Sq = 0.9890

h = 1.00            g = 0.35            t = 1.96

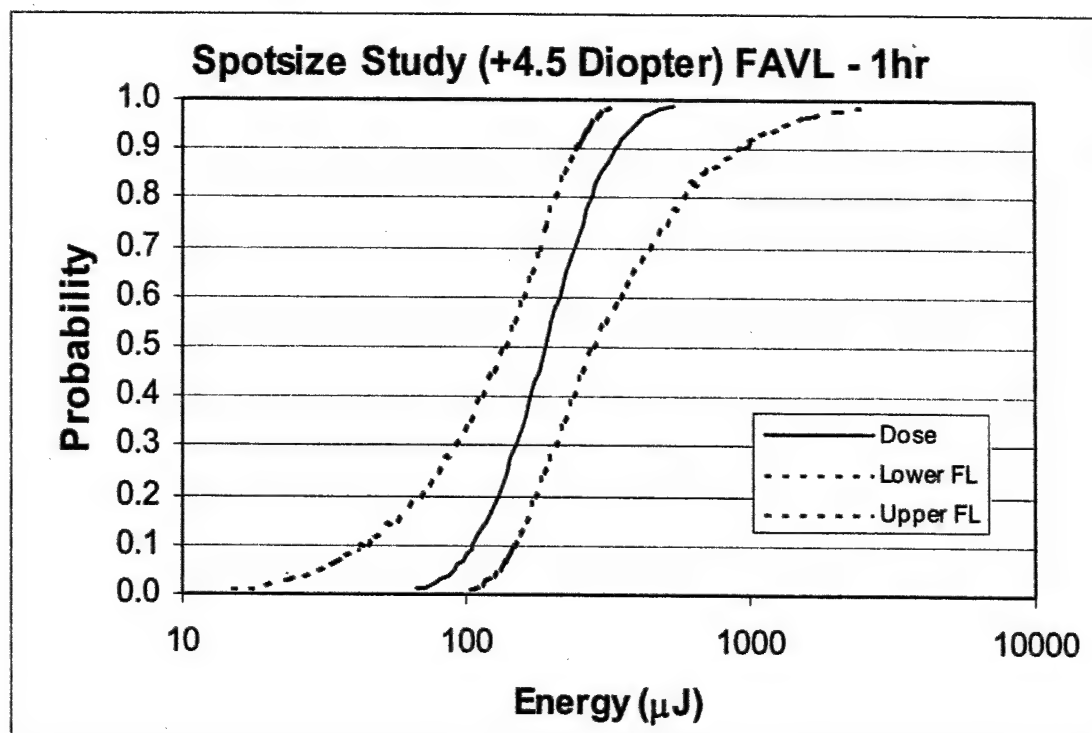
Log XBAR = 2.26    Log YBAR = 4.90

SYX = 30.517    SXY = 2.159    SXX = 0.421    S0 = 9.104

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	66.6	14.9	103.	0.55	200.	146.	306.
0.02	75.3	19.9	113.	0.60	212.	156.	340.
0.03	81.4	23.8	119.	0.65	225.	167.	381.
0.04	86.3	27.3	124.	0.70	239.	179.	432.
0.05	90.5	30.5	129.	0.75	256.	191.	497.
0.06	94.2	33.4	133.	0.80	276.	204.	584.
0.07	97.6	36.3	136.	0.85	301.	220.	708.
0.08	101.	39.0	140.	0.90	336.	240.	909.
0.09	104.	41.6	143.	0.91	345.	245.	966.
0.10	106.	44.2	146.	0.92	355.	251.	1.03e+003
0.15	119.	56.4	160.	0.93	367.	257.	1.11e+003
0.20	130.	68.0	174.	0.94	380.	264.	1.21e+003
0.25	140.	79.4	187.	0.95	396.	271.	1.33e+003
0.30	150.	90.7	202.	0.96	415.	281.	1.48e+003
0.35	159.	102.	217.	0.97	440.	293.	1.70e+003
0.40	169.	113.	235.	0.98	475.	309.	2.04e+003
0.45	179.	124.	255.	0.99	537.	337.	2.73e+003
0.50	189.	135.	279.				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
7.30	1	0	60.0	2	0	180.	1	0
8.00	1	0	61.0	1	0	204.	1	1
12.0	1	0	64.0	1	0	209.	1	1
14.0	1	0	73.0	1	0	232.	1	1
20.0	1	0	80.0	1	0	238.	1	1

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
31.0	1	0	88.0	1	0	283.	1	0
36.0	1	0	91.0	2	0	302.	1	1
37.0	1	0	96.0	1	0	320.	1	1
43.0	1	0	103.	1	0	322.	1	0
45.0	1	0	108.	1	0	394.	1	1
50.0	1	0	118.	1	0	416.	1	1
55.0	1	0	165.	1	1	426.	1	1
57.0	1	0	167.	1	1			
<b>Totals</b>							<b>40</b>	<b>11</b>



**Spotsize Study (+4.5 Diopter) FAVL - 24hr**  
**C77 OS, C77 OD, C65 OS**

ONES = 10                      ZEROES = 30                      TOTAL = 40

Percent confidence = 0.95

ED50 = 205.    Upper FL = 309.                      Lower FL = 145.

Intercept = -11.7                      Slope = 5.05

Pearson's Chi-Sq = 17.5605    Probability of Chi-Sq = 0.9958

h = 1.00                      g = 0.38                      t = 1.96

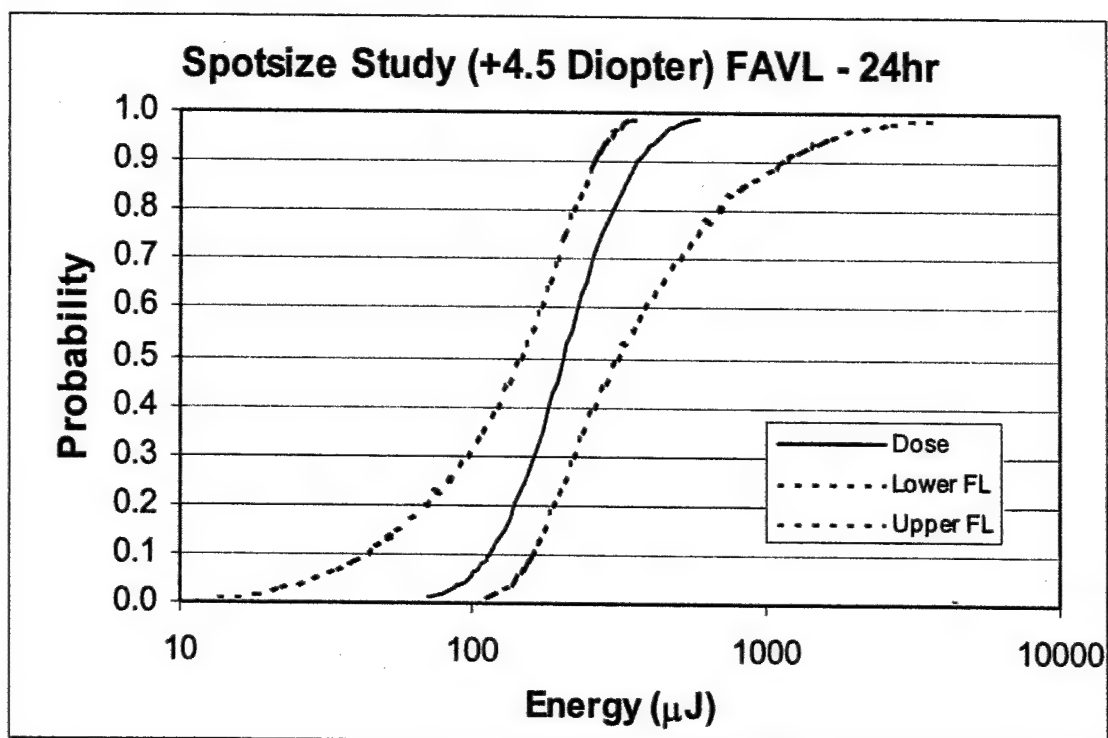
Log XBAR = 2.29                      Log YBAR = 4.88

SYX = 27.771    SXY = 2.022    SXX = 0.401    S0 = 9.086

<u>Prob</u>	<u>Dose</u>	<u>LFL</u>	<u>UFL</u>	<u>Prob</u>	<u>Dose</u>	<u>LFL</u>	<u>UFL</u>
0.01	70.8	13.4	111.	0.55	217.	157.	343.
0.02	80.2	18.3	121.	0.60	230.	169.	384.
0.03	86.8	22.3	128.	0.65	244.	181.	435.
0.04	92.1	25.8	134.	0.70	260.	193.	498.
0.05	96.7	29.1	139.	0.75	278.	206.	581.
0.06	101.	32.2	143.	0.80	300.	221.	693.
0.07	104.	35.2	147.	0.85	328.	238.	856.
0.08	108.	38.0	151.	0.90	367.	260.	1.12e+003
0.09	111.	40.8	154.	0.91	377.	265.	1.20e+003
0.10	114.	43.6	158.	0.92	388.	271.	1.29e+003
0.15	128.	56.8	173.	0.93	401.	277.	1.40e+003
0.20	139.	69.6	188.	0.94	416.	285.	1.53e+003
0.25	150.	82.3	203.	0.95	433.	293.	1.69e+003
0.30	161.	95.0	219.	0.96	455.	303.	1.91e+003
0.35	172.	108.	237.	0.97	483.	316.	2.21e+003
0.40	182.	120.	257.	0.98	522.	334.	2.70e+003
0.45	193.	133.	281.	0.99	591.	363.	3.69e+003
0.50	205.	145.	309.				

<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>
7.30	1	0	60.0	2	0	180.	1	0
8.00	1	0	61.0	1	0	204.	1	0
12.0	1	0	64.0	1	0	209.	1	1
14.0	1	0	73.0	1	0	232.	1	1
20.0	1	0	80.0	1	0	238.	1	1

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
31.0	1	0	88.0	1	0	283.	1	0
36.0	1	0	91.0	2	0	302.	1	1
37.0	1	0	96.0	1	0	320.	1	1
43.0	1	0	103.	1	0	322.	1	0
45.0	1	0	108.	1	0	394.	1	1
50.0	1	0	118.	1	0	416.	1	1
55.0	1	0	165.	1	1	426.	1	1
57.0	1	0	167.	1	1			
<b>Totals</b>							<b>40</b>	<b>10</b>





**Mac/Para Study (Mac-Combined) MVL - 1Hr**  
C52 OD, D01 OS, C87 OS, D01 OD, B84 OS, B84 OD

ONES = 55                      ZEROES = 58                      TOTAL = 113

Percent confidence = 0.95

ED50 = 0.401    Upper FL = 0.532                      Lower FL = 0.300

Intercept = 0.945                      Slope = 2.38

Pearson's Chi-Sq = 94.7132    Probability of Chi-Sq = 0.5752

h = 1.00                      g = 0.12                      t = 1.96

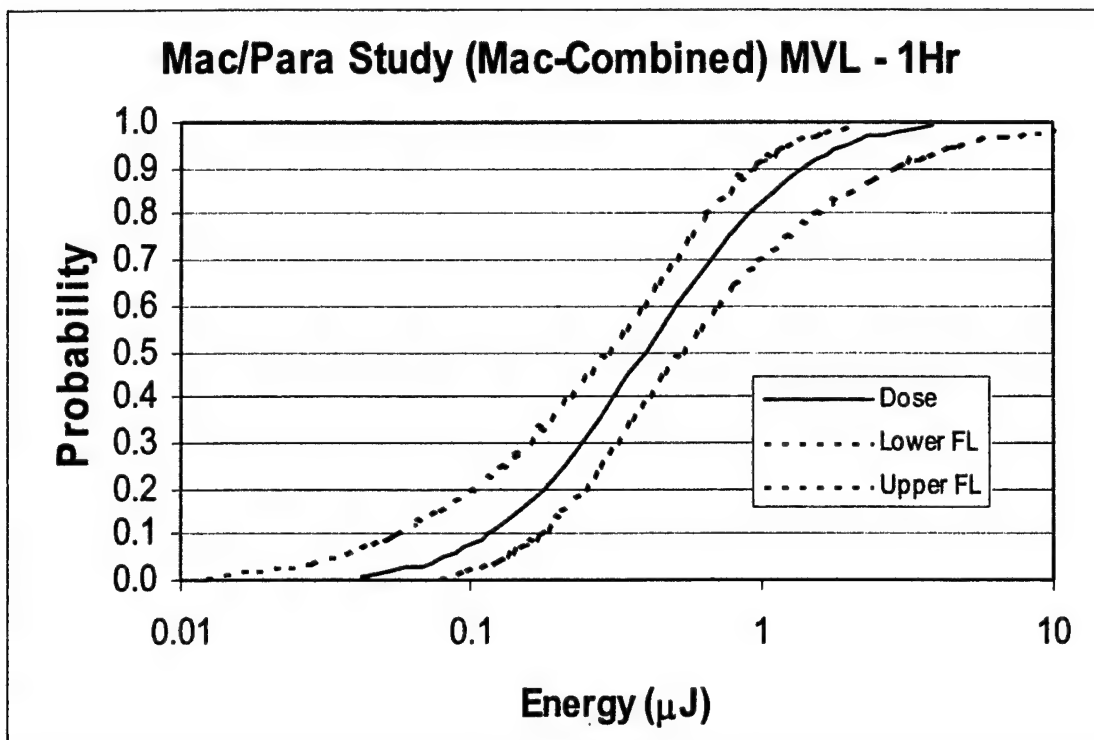
Log XBAR = -0.388                      Log YBAR = 5.02

SYX = 127.160                      SXY = 13.635    SXX = 5.730    S0 = 49.696

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.0422	0.0123	0.0790	0.55	0.453	0.344	0.613
0.02	0.0549	0.0182	0.0966	0.60	0.512	0.391	0.712
0.03	0.0650	0.0234	0.110	0.65	0.582	0.444	0.839
0.04	0.0737	0.0283	0.121	0.70	0.666	0.504	1.00
0.05	0.0816	0.0329	0.131	0.75	0.770	0.574	1.22
0.06	0.0891	0.0375	0.140	0.80	0.905	0.660	1.54
0.07	0.0961	0.0420	0.149	0.85	1.09	0.773	2.01
0.08	0.103	0.0465	0.157	0.90	1.39	0.936	2.84
0.09	0.110	0.0509	0.165	0.91	1.47	0.980	3.09
0.10	0.116	0.0554	0.173	0.92	1.56	1.03	3.39
0.15	0.147	0.0784	0.210	0.93	1.67	1.09	3.75
0.20	0.178	0.103	0.245	0.94	1.80	1.15	4.20
0.25	0.209	0.129	0.281	0.95	1.97	1.24	4.78
0.30	0.241	0.158	0.320	0.96	2.18	1.34	5.57
0.35	0.276	0.189	0.362	0.97	2.47	1.48	6.73
0.40	0.314	0.223	0.411	0.98	2.92	1.68	8.64
0.45	0.355	0.260	0.466	0.99	3.81	2.05	12.8
0.50	0.401	0.300	0.532				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0100	1	0	0.278	1	1	0.690	1	0
0.0200	3	0	0.280	2	0	0.700	1	1
0.0350	1	0	0.283	1	1	0.750	1	1
0.0400	1	0	0.290	1	0	0.760	1	1
0.0460	1	0	0.294	1	1	0.770	1	1

<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>
0.0470	1	0	0.295	1	0	0.800	1	0
0.0600	1	0	0.300	1	0	0.810	1	1
0.0680	1	0	0.303	1	0	0.820	1	1
0.0700	1	0	0.330	2	1	0.862	1	1
0.0720	1	0	0.350	2	1	0.870	1	1
0.0760	1	0	0.357	1	1	0.930	1	0
0.0970	1	0	0.370	2	1	0.950	1	1
0.0980	1	0	0.372	1	0	0.960	1	1
0.0990	1	0	0.376	1	1	0.961	1	1
0.100	2	0	0.381	1	1	0.980	1	0
0.101	1	0	0.433	1	1	1.03	1	1
0.107	1	1	0.440	2	1	1.09	1	1
0.125	1	0	0.450	1	1	1.22	1	0
0.140	3	0	0.490	1	0	1.23	1	1
0.150	2	0	0.497	1	1	1.24	1	1
0.153	1	0	0.500	1	0	1.25	1	1
0.160	1	0	0.530	1	1	1.34	1	1
0.164	2	0	0.540	1	1	1.72	1	1
0.177	1	0	0.544	1	1	1.74	1	0
0.180	1	0	0.560	1	1	1.90	1	1
0.196	1	1	0.570	1	1	1.97	1	1
0.216	1	0	0.600	1	1	1.97	1	1
0.225	1	1	0.617	1	0	2.10	1	1
0.230	1	0	0.630	2	0	2.21	1	1
0.234	1	0	0.649	1	1	2.33	1	1
0.240	1	1	0.650	1	1	2.34	1	1
0.260	1	0	0.658	1	1	3.16	1	1
0.277	1	0	0.680	1	1	3.30	1	1
<b>Totals</b>							<b>113</b>	<b>55</b>



**Mac/Para Study (Mac-Combined) MVL - 24Hr**  
**C52 OD, D01 OS, C87 OS, D01 OD, B84 OS, B84 OD**

ONES = 59                      ZEROES = 54                      TOTAL = 113

Percent confidence = 0.95

ED50 = 0.350 Upper FL = 0.461      Lower FL = 0.260

Intercept = 1.09              Slope = 2.40

Pearson's Chi-Sq = 88.7558      Probability of Chi-Sq = 0.7370

h = 1.00              g = 0.12              t = 1.96

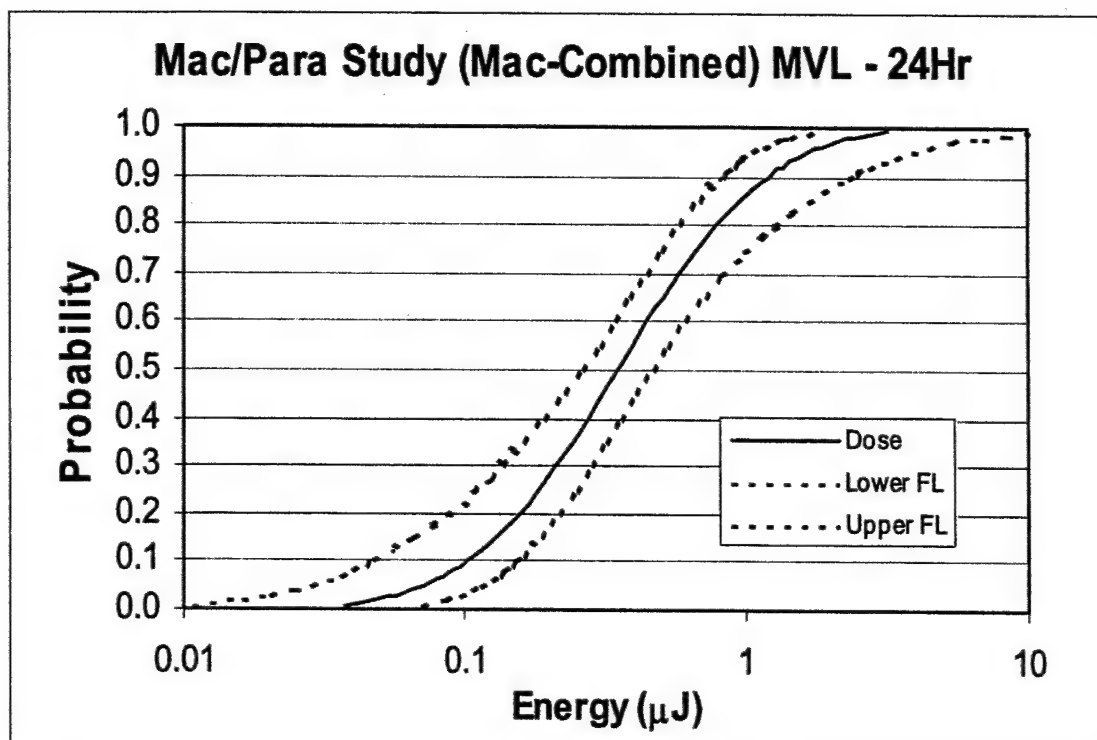
Log XBAR = -0.419              Log YBAR = 5.09

SYX = 121.617              SXY = 13.684 SXX = 5.698      S0 = 49.176

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.0376	0.0108	0.0709	0.55	0.395	0.298	0.528
0.02	0.0489	0.0160	0.0867	0.60	0.446	0.340	0.610
0.03	0.0577	0.0205	0.0985	0.65	0.507	0.387	0.714
0.04	0.0653	0.0247	0.108	0.70	0.579	0.441	0.849
0.05	0.0723	0.0287	0.117	0.75	0.668	0.503	1.03
0.06	0.0788	0.0326	0.126	0.80	0.785	0.579	1.29
0.07	0.0850	0.0365	0.133	0.85	0.946	0.678	1.68
0.08	0.0910	0.0404	0.140	0.90	1.20	0.822	2.36
0.09	0.0968	0.0442	0.147	0.91	1.27	0.860	2.56
0.10	0.102	0.0481	0.154	0.92	1.35	0.904	2.80
0.15	0.130	0.0678	0.186	0.93	1.44	0.954	3.10
0.20	0.156	0.0887	0.217	0.94	1.55	1.01	3.46
0.25	0.183	0.111	0.249	0.95	1.69	1.08	3.93
0.30	0.212	0.136	0.282	0.96	1.88	1.17	4.57
0.35	0.242	0.163	0.319	0.97	2.13	1.29	5.50
0.40	0.275	0.192	0.359	0.98	2.51	1.47	7.04
0.45	0.310	0.225	0.406	0.99	3.26	1.80	10.4
0.50	0.350	0.260	0.461				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0100	1	0	0.278	1	1	0.690	1	0
0.0200	3	0	0.280	2	1	0.700	1	0
0.0350	1	0	0.283	1	1	0.750	1	1
0.0400	1	0	0.290	1	1	0.760	1	1
0.0460	1	0	0.294	1	1	0.770	1	1

<b>Dose</b>	<b>Tries</b>	<b>Hits</b>	<b>Dose</b>	<b>Tries</b>	<b>Hits</b>	<b>Dose</b>	<b>Tries</b>	<b>Hits</b>
0.0470	1	0	0.295	1	0	0.800	1	1
0.0600	1	0	0.300	1	1	0.810	1	1
0.0680	1	0	0.303	1	0	0.820	1	0
0.0700	1	0	0.330	2	1	0.862	1	1
0.0720	1	0	0.350	2	0	0.870	1	0
0.0760	1	0	0.357	1	1	0.930	1	0
0.0970	1	0	0.370	2	1	0.950	1	1
0.0980	1	0	0.372	1	0	0.960	1	1
0.0990	1	0	0.376	1	1	0.961	1	1
0.100	2	0	0.381	1	1	0.980	1	0
0.101	1	0	0.433	1	1	1.03	1	1
0.107	1	1	0.440	2	2	1.09	1	1
0.125	1	0	0.450	1	0	1.22	1	0
0.140	3	0	0.490	1	0	1.23	1	1
0.150	2	1	0.497	1	1	1.24	1	1
0.153	1	0	0.500	1	1	1.25	1	1
0.160	1	0	0.530	1	1	1.34	1	1
0.164	2	0	0.540	1	1	1.72	1	1
0.177	1	0	0.544	1	1	1.74	1	1
0.180	1	0	0.560	1	1	1.90	1	1
0.196	1	1	0.570	1	1	1.97	1	1
0.216	1	0	0.600	1	1	1.97	1	1
0.225	1	1	0.617	1	0	2.10	1	1
0.230	1	0	0.630	2	2	2.21	1	1
0.234	1	0	0.649	1	1	2.33	1	1
0.240	1	0	0.650	1	1	2.34	1	1
0.260	1	0	0.658	1	1	3.16	1	1
0.277	1	0	0.680	1	1	3.30	1	1
<b>Totals</b>							<b>113</b>	<b>59</b>



**Mac/Para Study (Para-Combined) MVL - 1Hr**  
**C52 OD, D01 OS, C87 OS, D01 OD, B84 OS, B84 OD**

ONES = 44                      ZEROES = 78                      TOTAL = 122

Percent confidence = 0.95

ED50 = 0.649 Upper FL = 0.906      Lower FL = 0.505

Intercept = 0.445      Slope = 2.37

Pearson's Chi-Sq = 104.2023 Probability of Chi-Sq = 0.5585

h = 1.00      g = 0.15      t = 1.96

Log XBAR = -0.292                      Log YBAR = 4.75

SYX = 129.924      SXY = 10.861 SXX = 4.586      S0 = 58.109

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.0676	0.0182	0.124	0.55	0.733	0.569	1.07
0.02	0.0881	0.0278	0.150	0.60	0.830	0.637	1.28
0.03	0.104	0.0365	0.171	0.65	0.944	0.713	1.55
0.04	0.118	0.0446	0.188	0.70	1.08	0.798	1.90
0.05	0.131	0.0526	0.203	0.75	1.25	0.897	2.38
0.06	0.143	0.0604	0.217	0.80	1.47	1.02	3.07
0.07	0.155	0.0683	0.230	0.85	1.78	1.18	4.15
0.08	0.166	0.0761	0.242	0.90	2.26	1.42	6.06
0.09	0.176	0.0840	0.254	0.91	2.39	1.48	6.64
0.10	0.187	0.0919	0.266	0.92	2.54	1.55	7.34
0.15	0.237	0.133	0.322	0.93	2.72	1.63	8.19
0.20	0.286	0.177	0.377	0.94	2.94	1.73	9.27
0.25	0.337	0.225	0.436	0.95	3.21	1.84	10.7
0.30	0.390	0.276	0.500	0.96	3.56	1.99	12.6
0.35	0.446	0.330	0.575	0.97	4.04	2.18	15.4
0.40	0.507	0.386	0.664	0.98	4.78	2.47	20.2
0.45	0.574	0.445	0.773	0.99	6.23	3.01	31.1
0.50	0.649	0.505	0.906				

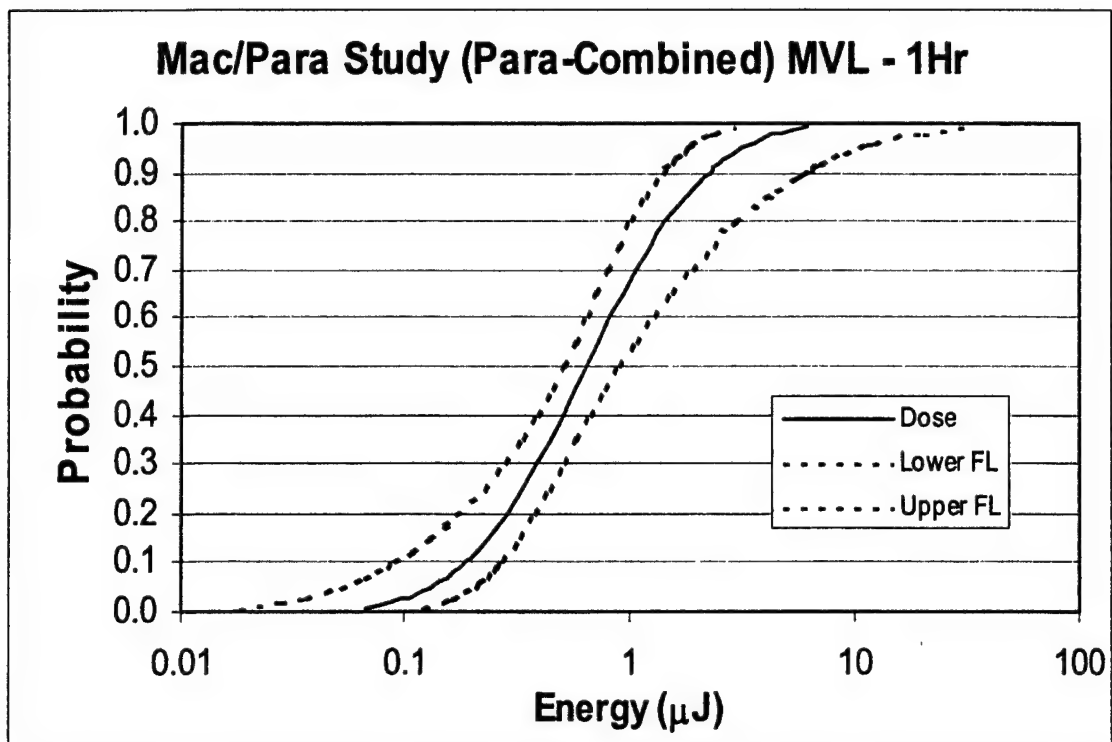
Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0340	1	0	0.310	2	1	0.600	1	1
0.0400	2	0	0.314	1	0	0.610	1	1
0.0470	1	0	0.320	2	1	0.619	1	0
0.0490	1	0	0.321	1	0	0.639	1	1
0.0500	1	0	0.322	1	0	0.640	1	1

<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>
0.0530	1	0	0.360	1	0	0.659	1	1
0.0670	1	0	0.370	1	0	0.670	1	0
0.0710	1	0	0.375	1	0	0.680	1	1
0.0770	1	0	0.378	1	0	0.690	2	0
0.0840	1	0	0.380	1	0	0.710	1	0
0.0990	1	0	0.384	1	0	0.770	1	1
0.100	1	0	0.390	1	0	0.780	1	1
0.108	1	0	0.400	1	0	0.825	2	2
0.110	1	0	0.419	1	0	0.837	1	0
0.124	1	0	0.420	2	0	0.850	1	1
0.145	1	0	0.428	1	1	0.888	1	0
0.150	1	1	0.444	1	1	0.890	1	0
0.162	1	0	0.446	1	0	0.930	1	1
0.170	1	0	0.460	1	0	0.950	1	0
0.179	1	1	0.461	1	0	1.01	1	0
0.181	1	0	0.466	1	0	1.02	1	1
0.200	1	0	0.470	1	0	1.05	1	1
0.201	1	1	0.480	1	0	1.13	1	1
0.202	1	0	0.490	1	0	1.19	1	1
0.210	1	0	0.500	2	1	1.27	1	1
0.220	1	1	0.503	1	0	1.31	1	0
0.228	1	0	0.520	2	0	1.32	1	1
0.230	2	0	0.522	1	1	1.34	1	1
0.231	2	0	0.530	1	0	1.42	1	1
0.240	1	0	0.538	1	1	1.57	1	1
0.250	1	0	0.543	2	1	1.84	1	1
0.269	1	0	0.561	1	0	1.87	1	1
0.270	1	0	0.564	1	1	1.98	1	1
0.278	1	0	0.570	2	0	2.16	1	1
0.297	1	1	0.580	1	1	2.25	1	1
0.300	2	1	0.598	1	0	2.41	1	1

**Totals**

**122 44**





**Mac/Para Study (Para-Combined) MVL - 24Hr**  
C52 OD, D01 OS, C87 OS, D01 OD, B84 OS, B84 OD

ONES = 49                      ZEROES = 73                      TOTAL = 122

Percent confidence = 0.95

ED50 = 0.554 Upper FL = 0.732      Lower FL = 0.436

Intercept = 0.650      Slope = 2.53

Pearson's Chi-Sq = 102.4975 Probability of Chi-Sq = 0.6313

h = 1.00              g = 0.14              t = 1.96

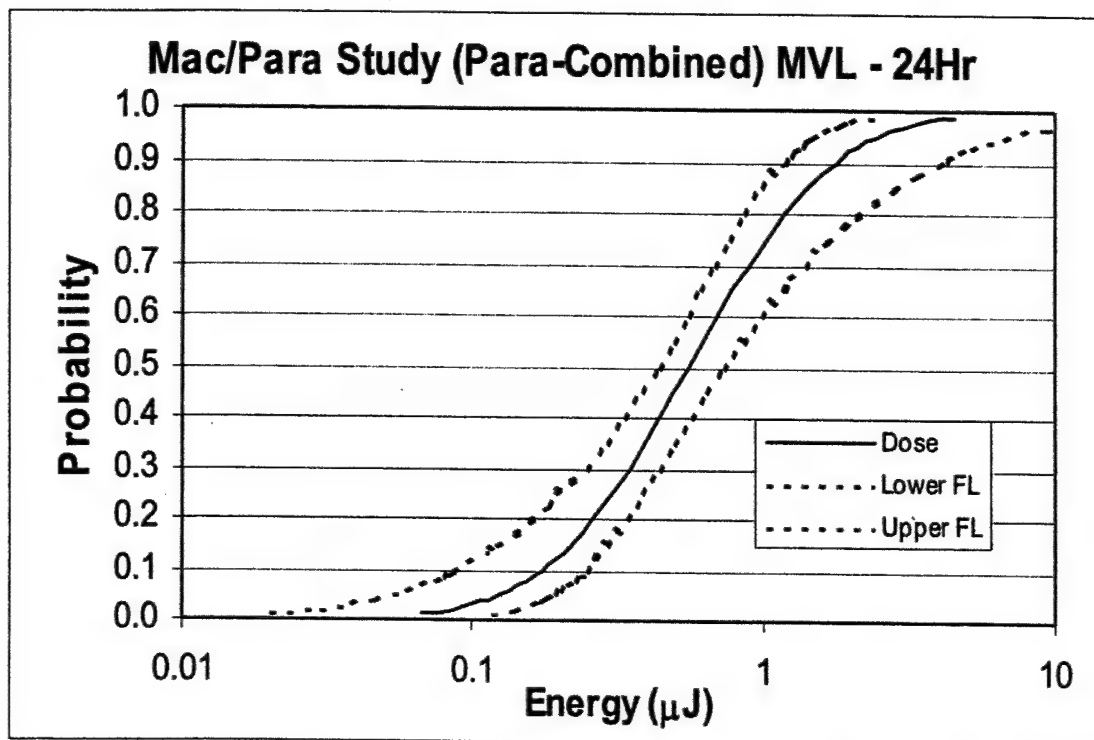
Log XBAR = -0.315                      Log YBAR = 4.85

SYY = 130.748              SXY = 11.159 SXX = 4.408      S0 = 57.564

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.0667	0.0202	0.118	0.55	0.621	0.491	0.848
0.02	0.0855	0.0298	0.142	0.60	0.697	0.549	0.993
0.03	0.100	0.0380	0.160	0.65	0.786	0.612	1.18
0.04	0.113	0.0457	0.175	0.70	0.892	0.683	1.41
0.05	0.124	0.0531	0.189	0.75	1.02	0.766	1.73
0.06	0.135	0.0602	0.201	0.80	1.19	0.866	2.17
0.07	0.145	0.0673	0.212	0.85	1.42	0.996	2.84
0.08	0.154	0.0743	0.223	0.90	1.78	1.18	4.01
0.09	0.164	0.0813	0.234	0.91	1.87	1.23	4.35
0.10	0.173	0.0882	0.244	0.92	1.99	1.29	4.77
0.15	0.216	0.124	0.291	0.93	2.12	1.36	5.27
0.20	0.257	0.161	0.337	0.94	2.28	1.43	5.89
0.25	0.300	0.201	0.385	0.95	2.47	1.52	6.69
0.30	0.344	0.243	0.436	0.96	2.72	1.64	7.77
0.35	0.390	0.288	0.493	0.97	3.06	1.79	9.35
0.40	0.440	0.335	0.559	0.98	3.58	2.02	12.0
0.45	0.494	0.385	0.638	0.99	4.59	2.42	17.7
0.50	0.554	0.436	0.732				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0340	1	0	0.310	2	1	0.610	1	1
0.0400	2	0	0.314	1	0	0.619	1	0
0.0470	1	0	0.320	2	1	0.639	1	1
0.0490	1	0	0.321	1	0	0.640	1	0
0.0500	1	0	0.322	1	0	0.659	1	1

<b>Dose</b>	<b>Tries</b>	<b>Hits</b>	<b>Dose</b>	<b>Tries</b>	<b>Hits</b>	<b>Dose</b>	<b>Tries</b>	<b>Hits</b>
0.0530	1	0	0.360	1	0	0.670	1	1
0.0670	1	0	0.370	1	0	0.680	1	1
0.0710	1	0	0.375	1	0	0.690	1	0
0.0770	1	0	0.378	1	0	0.710	1	0
0.0840	1	0	0.380	1	1	0.770	1	1
0.0900	1	0	0.384	1	0	0.780	1	1
0.0990	1	0	0.390	1	0	0.825	2	2
0.100	1	0	0.400	1	0	0.837	1	0
0.108	1	0	0.419	1	0	0.850	1	1
0.110	1	0	0.420	2	0	0.888	1	0
0.124	1	0	0.428	1	1	0.890	1	1
0.145	1	0	0.444	1	1	0.930	1	1
0.150	1	1	0.446	1	0	0.950	1	0
0.162	1	0	0.460	1	0	1.01	1	0
0.170	1	0	0.461	1	0	1.02	1	1
0.179	1	1	0.466	1	0	1.05	1	1
0.181	1	0	0.470	1	0	1.13	1	1
0.200	1	0	0.480	1	0	1.19	1	1
0.201	1	1	0.490	1	1	1.27	1	1
0.202	1	0	0.500	2	0	1.31	1	0
0.210	1	0	0.503	1	0	1.32	1	1
0.220	1	1	0.520	2	0	1.34	1	1
0.228	1	0	0.522	1	1	1.42	1	1
0.230	2	0	0.530	1	1	1.57	1	1
0.231	2	0	0.538	1	1	1.84	1	1
0.240	1	0	0.543	2	1	1.87	1	1
0.250	1	0	0.561	1	0	1.98	1	1
0.269	1	0	0.564	1	1	2.16	1	1
0.270	1	0	0.570	2	2	2.25	1	1
0.278	1	0	0.580	1	1	2.41	1	1
0.297	1	1	0.598	1	0	2.49	1	1
0.300	2	1	0.600	1	1			
<b>Totals</b>							<b>122</b>	<b>49</b>



**Mac/Para Study (Comb-Combined) MVL - 1Hr**  
C52 OD, D01 OS, C87 OS, D01 OD, B84 OS, B84 OD

ONES = 99                      ZEROES = 136                      TOTAL = 235

Percent confidence = 0.95

ED50 = 0.521 Upper FL = 0.638      Lower FL = 0.433

Intercept = 0.657      Slope = 2.32

Pearson's Chi-Sq = 167.8582 Probability of Chi-Sq = 0.8391

h = 1.00      g = 0.07      t = 1.96

Log XBAR = -0.329                      Log YBAR = 4.89

SYX = 225.833                      SXY = 24.968 SXX = 10.753 S0 = 110.121

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.0519	0.0235	0.0839	0.55	0.591	0.491	0.735
0.02	0.0680	0.0337	0.104	0.60	0.670	0.554	0.853
0.03	0.0808	0.0423	0.120	0.65	0.764	0.626	1.00
0.04	0.0919	0.0502	0.133	0.70	0.877	0.708	1.19
0.05	0.102	0.0577	0.145	0.75	1.02	0.807	1.43
0.06	0.112	0.0649	0.156	0.80	1.20	0.930	1.77
0.07	0.121	0.0720	0.167	0.85	1.46	1.09	2.28
0.08	0.129	0.0789	0.177	0.90	1.86	1.34	3.14
0.09	0.138	0.0858	0.186	0.91	1.97	1.41	3.39
0.10	0.146	0.0927	0.196	0.92	2.10	1.48	3.68
0.15	0.187	0.127	0.240	0.93	2.25	1.57	4.04
0.20	0.226	0.163	0.284	0.94	2.44	1.67	4.48
0.25	0.267	0.201	0.328	0.95	2.66	1.80	5.05
0.30	0.310	0.241	0.376	0.96	2.96	1.96	5.80
0.35	0.356	0.284	0.429	0.97	3.37	2.18	6.89
0.40	0.406	0.330	0.488	0.98	4.00	2.50	8.66
0.45	0.460	0.380	0.557	0.99	5.24	3.11	12.4
0.50	0.521	0.433	0.638				

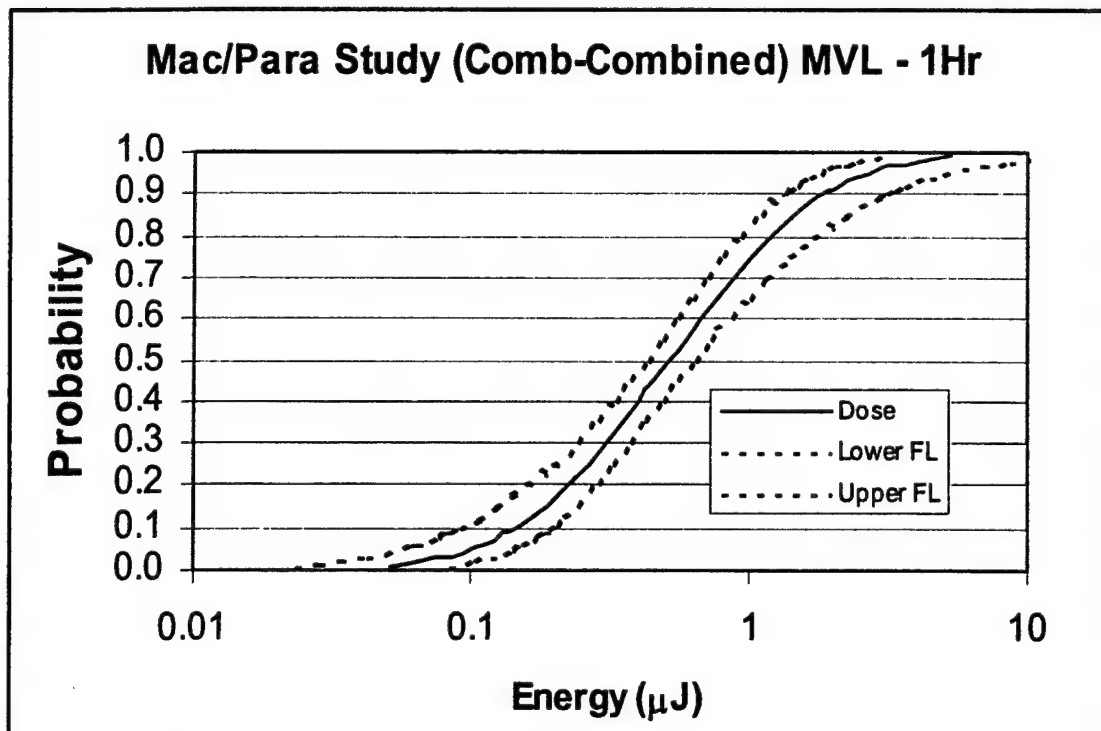
Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0100	1	0	0.294	1	1	0.658	1	1
0.0200	3	0	0.295	1	0	0.659	1	1
0.0340	1	0	0.297	1	1	0.670	1	0
0.0350	1	0	0.300	3	1	0.680	2	2
0.0400	3	0	0.303	1	0	0.690	3	0

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0460	1	0	0.310	2	1	0.700	1	1
0.0470	2	0	0.314	1	0	0.710	1	0
0.0490	1	0	0.320	2	1	0.750	1	1
0.0500	1	0	0.321	1	0	0.760	1	1
0.0530	1	0	0.322	1	0	0.770	2	2
0.0600	1	0	0.330	2	1	0.780	1	1
0.0670	1	0	0.350	2	1	0.800	1	0
0.0680	1	0	0.357	1	1	0.810	1	1
0.0700	1	0	0.360	1	0	0.820	1	1
0.0710	1	0	0.370	3	1	0.825	2	2
0.0720	1	0	0.372	1	0	0.837	1	0
0.0760	1	0	0.375	1	0	0.850	1	1
0.0770	1	0	0.376	1	1	0.862	1	1
0.0840	1	0	0.378	1	0	0.870	1	1
0.0970	1	0	0.380	1	0	0.888	1	0
0.0980	1	0	0.381	1	1	0.890	1	0
0.0990	2	0	0.384	1	0	0.930	2	1
0.100	3	0	0.390	1	0	0.950	2	1
0.101	1	0	0.400	1	0	0.960	1	1
0.107	1	1	0.419	1	0	0.961	1	1
0.108	1	0	0.420	2	0	0.980	1	0
0.110	1	0	0.428	1	1	1.01	1	0
0.124	1	0	0.433	1	1	1.02	1	1
0.125	1	0	0.440	2	1	1.03	1	1
0.140	3	0	0.444	1	1	1.05	1	1
0.145	1	0	0.446	1	0	1.09	1	1
0.150	3	1	0.450	1	1	1.13	1	1
0.153	1	0	0.460	1	0	1.19	1	1
0.160	1	0	0.461	1	0	1.22	1	0
0.162	1	0	0.466	1	0	1.23	1	1
0.164	2	0	0.470	1	0	1.24	1	1
0.170	1	0	0.480	1	0	1.25	1	1
0.177	1	0	0.490	2	0	1.27	1	1
0.179	1	1	0.497	1	1	1.31	1	0
0.180	1	0	0.500	3	1	1.32	1	1
0.181	1	0	0.503	1	0	1.34	1	1
0.196	1	1	0.520	2	0	1.34	1	1
0.200	1	0	0.522	1	1	1.42	1	1
0.201	1	1	0.530	2	1	1.57	1	1
0.202	1	0	0.538	1	1	1.72	1	1
0.210	1	0	0.540	1	1	1.74	1	0
0.216	1	0	0.543	2	1	1.84	1	1
0.220	1	1	0.544	1	1	1.87	1	1
0.225	1	1	0.560	1	1	1.90	1	1
0.228	1	0	0.561	1	0	1.97	1	1
0.230	3	0	0.564	1	1	1.97	1	1

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.231	2	0	0.570	3	1	1.98	1	1
0.234	1	0	0.580	1	1	2.10	1	1
0.240	2	1	0.598	1	0	2.16	1	1
0.250	1	0	0.600	2	2	2.21	1	1
0.260	1	0	0.610	1	1	2.25	1	1
0.269	1	0	0.617	1	0	2.33	1	1
0.270	1	0	0.619	1	0	2.34	1	1
0.277	1	0	0.630	2	0	2.41	1	1
0.278	2	1	0.639	1	1	2.49	1	1
0.280	2	0	0.640	1	1	3.16	1	1
0.283	1	1	0.649	1	1	3.30	1	1
0.290	1	0	0.650	1	1	3.88	1	1

Totals

235 99



**Mac/Para Study (Comb-Combined) MVL - 24Hr**  
**C52 OD, D01 OS, C87 OS, D01 OD, B84 OS, B84 OD**

ONES = 108 ZEROES = 127 TOTAL = 235

Percent confidence = 0.95

ED50 = 0.451 Upper FL = 0.545 Lower FL = 0.375

Intercept = 0.827 Slope = 2.39

Pearson's Chi-Sq = 171.7124 Probability of Chi-Sq = 0.7970

h = 1.00 g = 0.06 t = 1.96

Log XBAR = -0.356 Log YBAR = 4.97

SY Y = 232.663 SXY = 25.475 SXX = 10.647 S0 = 109.170

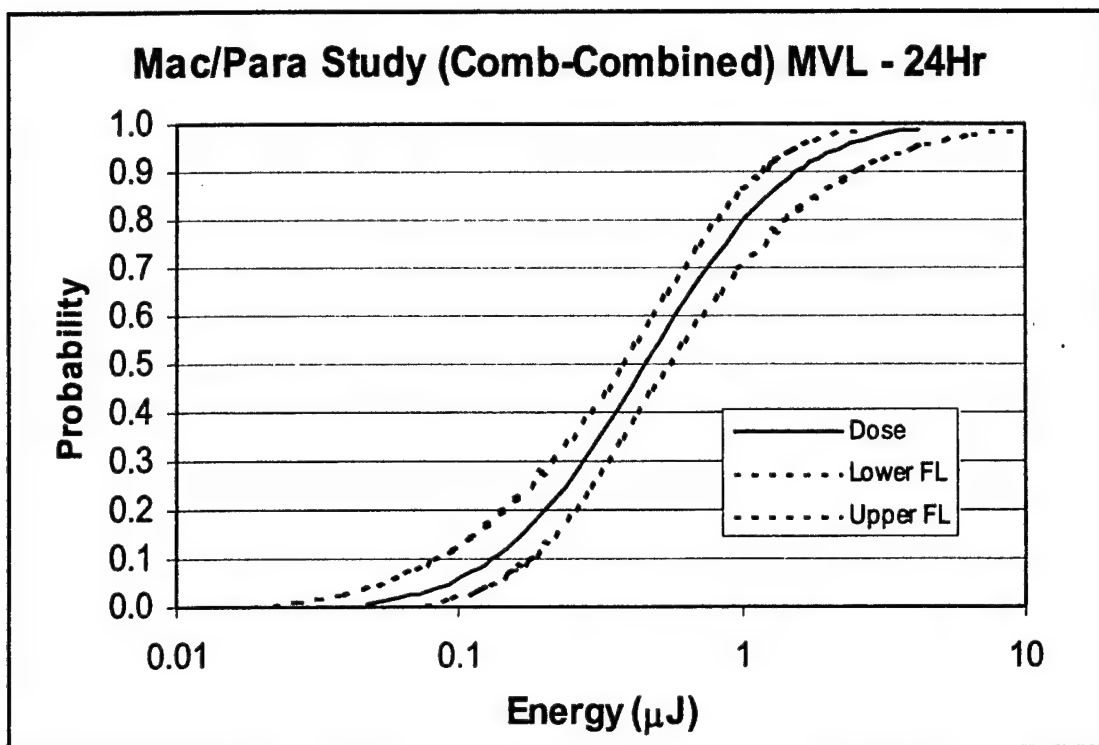
Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.0481	0.0222	0.0772	0.55	0.509	0.425	0.622
0.02	0.0625	0.0315	0.0955	0.60	0.576	0.480	0.716
0.03	0.0738	0.0392	0.109	0.65	0.654	0.542	0.832
0.04	0.0837	0.0462	0.121	0.70	0.747	0.613	0.979
0.05	0.0926	0.0528	0.132	0.75	0.863	0.697	1.17
0.06	0.101	0.0591	0.142	0.80	1.01	0.802	1.43
0.07	0.109	0.0653	0.151	0.85	1.22	0.941	1.82
0.08	0.117	0.0714	0.159	0.90	1.55	1.15	2.48
0.09	0.124	0.0774	0.168	0.91	1.64	1.20	2.67
0.10	0.131	0.0834	0.176	0.92	1.74	1.27	2.89
0.15	0.166	0.113	0.215	0.93	1.87	1.34	3.16
0.20	0.201	0.144	0.252	0.94	2.01	1.43	3.49
0.25	0.236	0.176	0.290	0.95	2.20	1.53	3.91
0.30	0.272	0.210	0.331	0.96	2.43	1.66	4.47
0.35	0.311	0.247	0.375	0.97	2.76	1.84	5.28
0.40	0.353	0.286	0.424	0.98	3.26	2.11	6.57
0.45	0.400	0.329	0.479	0.99	4.23	2.61	9.29
0.50	0.451	0.375	0.545				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0100	1	0	0.290	1	1	0.650	1	1
0.0200	3	0	0.294	1	1	0.658	1	1
0.0340	1	0	0.295	1	0	0.659	1	1
0.0350	1	0	0.297	1	1	0.670	1	1
0.0400	3	0	0.300	3	2	0.680	2	2



Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0460	1	0	0.303	1	0	0.690	2	0
0.0470	2	0	0.310	2	1	0.700	1	0
0.0490	1	0	0.314	1	0	0.710	1	0
0.0500	1	0	0.320	2	1	0.750	1	1
0.0530	1	0	0.321	1	0	0.760	1	1
0.0600	1	0	0.322	1	0	0.770	2	2
0.0670	1	0	0.330	2	1	0.780	1	1
0.0680	1	0	0.350	2	0	0.800	1	1
0.0700	1	0	0.357	1	1	0.810	1	1
0.0710	1	0	0.360	1	0	0.820	1	0
0.0720	1	0	0.370	3	1	0.825	2	2
0.0760	1	0	0.372	1	0	0.837	1	0
0.0770	1	0	0.375	1	0	0.850	1	1
0.0840	1	0	0.376	1	1	0.862	1	1
0.0900	1	0	0.378	1	0	0.870	1	0
0.0970	1	0	0.380	1	1	0.888	1	0
0.0980	1	0	0.381	1	1	0.890	1	1
0.0990	2	0	0.384	1	0	0.930	2	1
0.100	3	0	0.390	1	0	0.950	2	1
0.101	1	0	0.400	1	0	0.960	1	1
0.107	1	1	0.419	1	0	0.961	1	1
0.108	1	0	0.420	2	0	0.980	1	0
0.110	1	0	0.428	1	1	1.01	1	0
0.124	1	0	0.433	1	1	1.02	1	1
0.125	1	0	0.440	2	2	1.03	1	1
0.140	3	0	0.444	1	1	1.05	1	1
0.145	1	0	0.446	1	0	1.09	1	1
0.150	3	2	0.450	1	0	1.13	1	1
0.153	1	0	0.460	1	0	1.19	1	1
0.160	1	0	0.461	1	0	1.22	1	0
0.162	1	0	0.466	1	0	1.23	1	1
0.164	2	0	0.470	1	0	1.24	1	1
0.170	1	0	0.480	1	0	1.25	1	1
0.177	1	0	0.490	2	1	1.27	1	1
0.179	1	1	0.497	1	1	1.31	1	0
0.180	1	0	0.500	3	1	1.32	1	1
0.181	1	0	0.503	1	0	1.34	1	1
0.196	1	1	0.520	2	0	1.34	1	1
0.200	1	0	0.522	1	1	1.42	1	1
0.201	1	1	0.530	2	2	1.57	1	1
0.202	1	0	0.538	1	1	1.72	1	1
0.210	1	0	0.540	1	1	1.74	1	1
0.216	1	0	0.543	2	1	1.84	1	1
0.220	1	1	0.544	1	1	1.87	1	1
0.225	1	1	0.560	1	1	1.90	1	1
0.228	1	0	0.561	1	0	1.97	1	1

<b>Dose</b>	<b>Tries</b>	<b>Hits</b>	<b>Dose</b>	<b>Tries</b>	<b>Hits</b>	<b>Dose</b>	<b>Tries</b>	<b>Hits</b>
0.230	3	0	0.564	1	1	1.97	1	1
0.231	2	0	0.570	3	3	1.98	1	1
0.234	1	0	0.580	1	1	2.10	1	1
0.240	2	0	0.598	1	0	2.16	1	1
0.250	1	0	0.600	2	2	2.21	1	1
0.260	1	0	0.610	1	1	2.25	1	1
0.269	1	0	0.617	1	0	2.33	1	1
0.270	1	0	0.619	1	0	2.34	1	1
0.277	1	0	0.630	2	2	2.41	1	1
0.278	2	1	0.639	1	1	2.49	1	1
0.280	2	1	0.640	1	0	3.16	1	1
0.283	1	1	0.649	1	1	3.30	1	1
<b>Totals</b>							<b>235</b>	<b>108</b>



**Multipulse Study (1 Pulse - para) MVL - 1hr**  
**C52 OD, D01 OS, C87 OS, D01 OD, B84 OS, B84 OD**

ONES = 44                  ZEROES = 78                  TOTAL = 122

Percent confidence = 0.95

ED50 = 0.649 Upper FL = 0.906      Lower FL = 0.505

Intercept = 0.445      Slope = 2.37

Pearson's Chi-Sq = 104.2023 Probability of Chi-Sq = 0.5585

h = 1.00      g = 0.15      t = 1.96

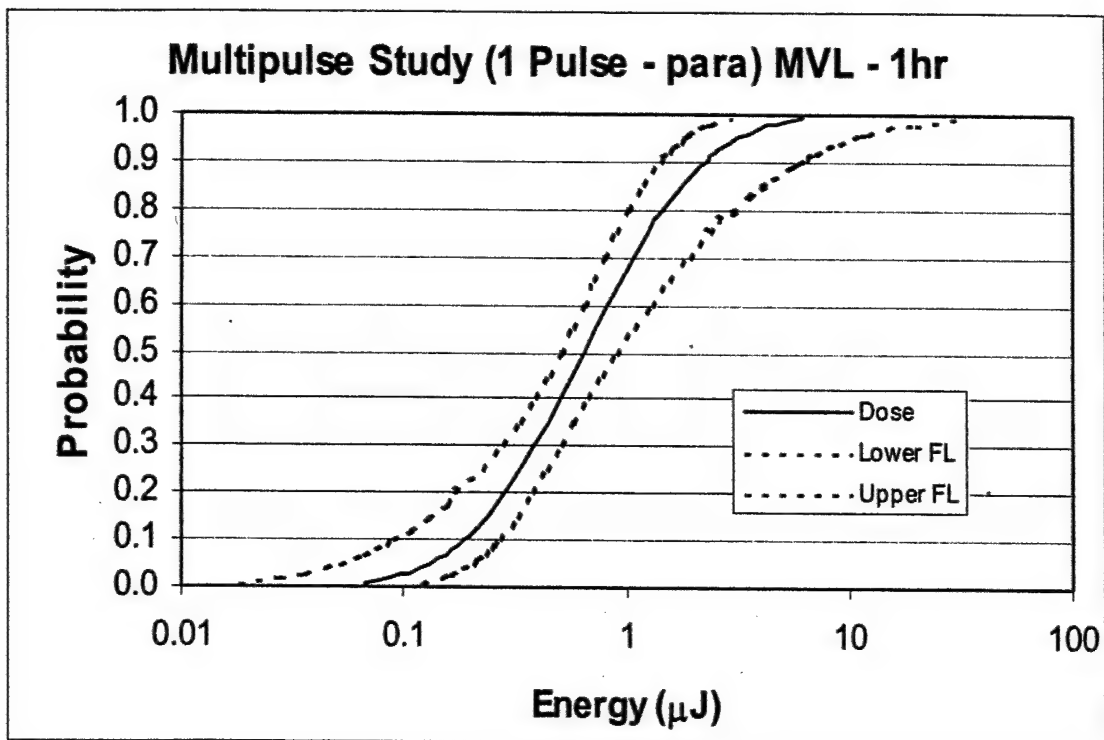
Log XBAR = -0.292                  Log YBAR = 4.75

SYY = 129.924      SXY = 10.861 SXX = 4.586      S0 = 58.109

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.0676	0.0182	0.124	0.55	0.733	0.569	1.07
0.02	0.0881	0.0278	0.150	0.60	0.830	0.637	1.28
0.03	0.104	0.0365	0.171	0.65	0.944	0.713	1.55
0.04	0.118	0.0446	0.188	0.70	1.08	0.798	1.90
0.05	0.131	0.0526	0.203	0.75	1.25	0.897	2.38
0.06	0.143	0.0604	0.217	0.80	1.47	1.02	3.07
0.07	0.155	0.0683	0.230	0.85	1.78	1.18	4.15
0.08	0.166	0.0761	0.242	0.90	2.26	1.42	6.06
0.09	0.176	0.0840	0.254	0.91	2.39	1.48	6.64
0.10	0.187	0.0919	0.266	0.92	2.54	1.55	7.34
0.15	0.237	0.133	0.322	0.93	2.72	1.63	8.19
0.20	0.286	0.177	0.377	0.94	2.94	1.73	9.27
0.25	0.337	0.225	0.436	0.95	3.21	1.84	10.7
0.30	0.390	0.276	0.500	0.96	3.56	1.99	12.6
0.35	0.446	0.330	0.575	0.97	4.04	2.18	15.4
0.40	0.507	0.386	0.664	0.98	4.78	2.47	20.2
0.45	0.574	0.445	0.773	0.99	6.23	3.01	31.1
0.50	0.649	0.505	0.906				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0340	1	0	0.310	2	1	0.600	1	1
0.0400	2	0	0.314	1	0	0.610	1	1
0.0470	1	0	0.320	2	1	0.619	1	0
0.0490	1	0	0.321	1	0	0.639	1	1
0.0500	1	0	0.322	1	0	0.640	1	1

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0530	1	0	0.360	1	0	0.659	1	1
0.0670	1	0	0.370	1	0	0.670	1	0
0.0710	1	0	0.375	1	0	0.680	1	1
0.0770	1	0	0.378	1	0	0.690	2	0
0.0840	1	0	0.380	1	0	0.710	1	0
0.0990	1	0	0.384	1	0	0.770	1	1
0.100	1	0	0.390	1	0	0.780	1	1
0.108	1	0	0.400	1	0	0.825	2	2
0.110	1	0	0.419	1	0	0.837	1	0
0.124	1	0	0.420	2	0	0.850	1	1
0.145	1	0	0.428	1	1	0.888	1	0
0.150	1	1	0.444	1	1	0.890	1	0
0.162	1	0	0.446	1	0	0.930	1	1
0.170	1	0	0.460	1	0	0.950	1	0
0.179	1	1	0.461	1	0	1.01	1	0
0.181	1	0	0.466	1	0	1.02	1	1
0.200	1	0	0.470	1	0	1.05	1	1
0.201	1	1	0.480	1	0	1.13	1	1
0.202	1	0	0.490	1	0	1.19	1	1
0.210	1	0	0.500	2	1	1.27	1	1
0.220	1	1	0.503	1	0	1.31	1	0
0.228	1	0	0.520	2	0	1.32	1	1
0.230	2	0	0.522	1	1	1.34	1	1
0.231	2	0	0.530	1	0	1.42	1	1
0.240	1	0	0.538	1	1	1.57	1	1
0.250	1	0	0.543	2	1	1.84	1	1
0.269	1	0	0.561	1	0	1.87	1	1
0.270	1	0	0.564	1	1	1.98	1	1
0.278	1	0	0.570	2	0	2.16	1	1
0.297	1	1	0.580	1	1	2.25	1	1
0.300	2	1	0.598	1	0	2.41	1	1
<b>Totals</b>							<b>122</b>	<b>44</b>



**Multipulse Study (1 Pulse - para) MVL - 24hr**  
C52 OD, D01 OS, C87 OS, D01 OD, B84 OS, B84 OD

ONES = 49                      ZEROES = 73                      TOTAL = 122

Percent confidence = 0.95

ED50 = 0.554 Upper FL = 0.732      Lower FL = 0.436

Intercept = 0.650      Slope = 2.53

Pearson's Chi-Sq = 102.4975 Probability of Chi-Sq = 0.6313

h = 1.00      g = 0.14      t = 1.96

Log XBAR = -0.315                      Log YBAR = 4.85

SYX = 130.748                      SXY = 11.159 SXX = 4.408      S0 = 57.564

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.0667	0.0202	0.118	0.55	0.621	0.491	0.848
0.02	0.0855	0.0298	0.142	0.60	0.697	0.549	0.993
0.03	0.100	0.0380	0.160	0.65	0.786	0.612	1.18
0.04	0.113	0.0457	0.175	0.70	0.892	0.683	1.41
0.05	0.124	0.0531	0.189	0.75	1.02	0.766	1.73
0.06	0.135	0.0602	0.201	0.80	1.19	0.866	2.17
0.07	0.145	0.0673	0.212	0.85	1.42	0.996	2.84
0.08	0.154	0.0743	0.223	0.90	1.78	1.18	4.01
0.09	0.164	0.0813	0.234	0.91	1.87	1.23	4.35
0.10	0.173	0.0882	0.244	0.92	1.99	1.29	4.77
0.15	0.216	0.124	0.291	0.93	2.12	1.36	5.27
0.20	0.257	0.161	0.337	0.94	2.28	1.43	5.89
0.25	0.300	0.201	0.385	0.95	2.47	1.52	6.69
0.30	0.344	0.243	0.436	0.96	2.72	1.64	7.77
0.35	0.390	0.288	0.493	0.97	3.06	1.79	9.35
0.40	0.440	0.335	0.559	0.98	3.58	2.02	12.0
0.45	0.494	0.385	0.638	0.99	4.59	2.42	17.7
0.50	0.554	0.436	0.732				

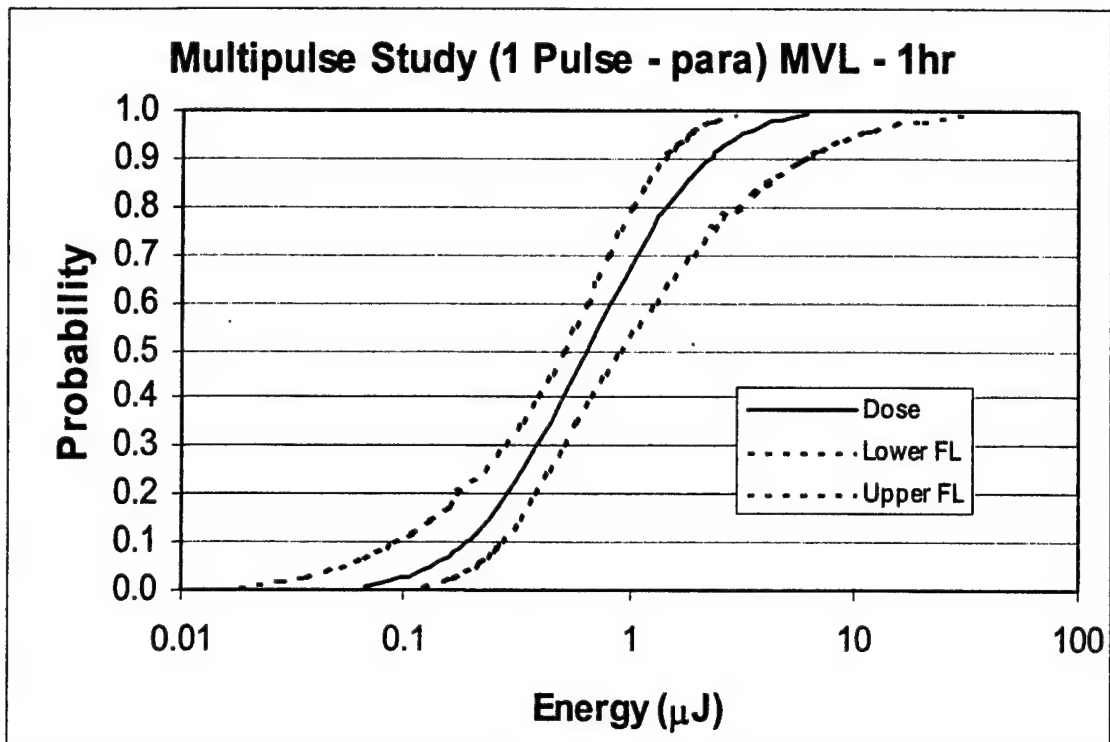
Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0340	1	0	0.310	2	1	0.610	1	1
0.0400	2	0	0.314	1	0	0.619	1	0
0.0470	1	0	0.320	2	1	0.639	1	1
0.0490	1	0	0.321	1	0	0.640	1	0
0.0500	1	0	0.322	1	0	0.659	1	1

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0530	1	0	0.360	1	0	0.670	1	1
0.0670	1	0	0.370	1	0	0.680	1	1
0.0710	1	0	0.375	1	0	0.690	1	0
0.0770	1	0	0.378	1	0	0.710	1	0
0.0840	1	0	0.380	1	1	0.770	1	1
0.0900	1	0	0.384	1	0	0.780	1	1
0.0990	1	0	0.390	1	0	0.825	2	2
0.100	1	0	0.400	1	0	0.837	1	0
0.108	1	0	0.419	1	0	0.850	1	1
0.110	1	0	0.420	2	0	0.888	1	0
0.124	1	0	0.428	1	1	0.890	1	1
0.145	1	0	0.444	1	1	0.930	1	1
0.150	1	1	0.446	1	0	0.950	1	0
0.162	1	0	0.460	1	0	1.01	1	0
0.170	1	0	0.461	1	0	1.02	1	1
0.179	1	1	0.466	1	0	1.05	1	1
0.181	1	0	0.470	1	0	1.13	1	1
0.200	1	0	0.480	1	0	1.19	1	1
0.201	1	1	0.490	1	1	1.27	1	1
0.202	1	0	0.500	2	0	1.31	1	0
0.210	1	0	0.503	1	0	1.32	1	1
0.220	1	1	0.520	2	0	1.34	1	1
0.228	1	0	0.522	1	1	1.42	1	1
0.230	2	0	0.530	1	1	1.57	1	1
0.231	2	0	0.538	1	1	1.84	1	1
0.240	1	0	0.543	2	1	1.87	1	1
0.250	1	0	0.561	1	0	1.98	1	1
0.269	1	0	0.564	1	1	2.16	1	1
0.270	1	0	0.570	2	2	2.25	1	1
0.278	1	0	0.580	1	1	2.41	1	1
0.297	1	1	0.598	1	0	2.49	1	1
0.300	2	1	0.600	1	1			

**Totals**

**122 49**





**Multipulse Study (1 Pulse - para) FAVL - 1hr**  
C52 OD, D01 OS, C87 OS, D01 OD, B84 OS, B84 OD

ONES = 10                      ZEROES = 112                      TOTAL = 122

Percent confidence = 0.95

ED50 = 13.2    Upper FL = 6.40e-005                      Lower FL = 1.90

Intercept = -1.09                      Slope = 0.976

Pearson's Chi-Sq = 192.8977    Probability of Chi-Sq = 0.0000

h = 1.79                      g = 1.80                      t = 1.98

Log XBAR = -0.244                      Log YBAR = 3.67

SYX = 196.804                      SXY = 4.003    SXX = 4.102    S0 = 34.334

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.0546	181.	0.649	0.55	17.8	0.526	0.000110
0.02	0.104	34.0	0.689	0.60	24.0	0.531	5.12e-005
0.03	0.156	11.3	0.741	0.65	32.8	0.535	2.32e-005
0.04	0.212	4.69	0.830	0.70	45.5	0.539	1.01e-005
0.05	0.272	1.86	1.12	0.75	64.9	0.542	4.13e-006
0.06	0.337	-1.#J	-1.#J	0.80	96.2	0.546	1.52e-006
0.07	0.406	-1.#J	-1.#J	0.85	152.	0.550	4.78e-007
0.08	0.480	-1.#J	-1.#J	0.90	272.	0.554	1.11e-007
0.09	0.558	-1.#J	-1.#J	0.91	312.	0.555	7.80e-008
0.10	0.642	-1.#J	-1.#J	0.92	364.	0.556	5.32e-008
0.15	1.14	-1.#J	-1.#J	0.93	430.	0.557	3.49e-008
0.20	1.81	0.421	0.0423	0.94	518.	0.558	2.18e-008
0.25	2.69	0.462	0.0143	0.95	640.	0.559	1.28e-008
0.30	3.83	0.483	0.00564	0.96	822.	0.561	6.81e-009
0.35	5.32	0.497	0.00240	0.97	1.12e+003	0.562	3.14e-009
0.40	7.26	0.507	0.00108	0.98	1.68e+003	0.564	1.12e-009
0.45	9.82	0.515	0.000499	0.99	3.20e+003	0.567	2.22e-010
0.50	13.2	0.521	0.000234				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0340	1	0	0.310	2	0	0.610	1	0
0.0400	2	0	0.314	1	0	0.619	1	0
0.0470	1	1	0.320	2	0	0.639	1	0
0.0490	1	0	0.321	1	1	0.640	1	0
0.0500	1	0	0.322	1	0	0.659	1	0

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0530	1	0	0.360	1	0	0.670	1	0
0.0670	1	0	0.370	1	0	0.680	1	0
0.0710	1	0	0.375	1	0	0.690	1	0
0.0770	1	0	0.378	1	0	0.710	1	0
0.0840	1	0	0.380	1	0	0.770	1	0
0.0900	1	0	0.384	1	0	0.780	1	0
0.0990	1	0	0.390	1	0	0.825	2	0
0.100	1	0	0.400	1	0	0.837	1	0
0.108	1	0	0.419	1	0	0.850	1	0
0.110	1	0	0.420	2	0	0.888	1	0
0.124	1	0	0.428	1	0	0.890	1	0
0.145	1	0	0.444	1	0	0.930	1	0
0.150	1	0	0.446	1	0	0.950	1	0
0.162	1	0	0.460	1	0	1.01	1	0
0.170	1	0	0.461	1	0	1.02	1	0
0.179	1	0	0.466	1	0	1.05	1	0
0.181	1	0	0.470	1	0	1.13	1	0
0.200	1	0	0.480	1	1	1.19	1	0
0.201	1	0	0.490	1	1	1.27	1	1
0.202	1	0	0.500	2	0	1.31	1	0
0.210	1	0	0.503	1	0	1.32	1	1
0.220	1	0	0.520	2	0	1.34	1	1
0.228	1	0	0.522	1	0	1.42	1	0
0.230	2	0	0.530	1	0	1.57	1	1
0.231	2	0	0.538	1	0	1.84	1	0
0.240	1	0	0.543	2	0	1.87	1	0
0.250	1	0	0.561	1	0	1.98	1	0
0.269	1	0	0.564	1	0	2.16	1	1
0.270	1	0	0.570	2	0	2.25	1	0
0.278	1	0	0.580	1	0	2.41	1	0
0.297	1	0	0.598	1	0	2.49	1	1
0.300	2	0	0.600	1	0			

**Totals**

**122**

**10**

**Multipulse Study (1 Pulse - para) FAVL - 24hr**  
**C52 OD, D01 OS, C87 OS, D01 OD, B84 OS, B84 OD**

ONES = 6                      ZEROES = 116                      TOTAL = 122

Percent confidence = 0.95

ED50 = 26.9    Upper FL = 0.0177    Lower FL = 1.80

Intercept = -1.38              Slope = 0.964

Pearson's Chi-Sq = 297.5283    Probability of Chi-Sq = 0.0000

h = 2.75              g = 4.09              t = 1.98

Log XBAR = -0.216              Log YBAR = 3.41

SYX = 300.173              SXY = 2.745    SXX = 2.849    S0 = 24.728

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.104	1.67	0.694	0.55	36.3	0.739	0.0355
0.02	0.199	-1.#J	-1.#J	0.60	49.3	0.760	0.0283
0.03	0.300	-1.#J	-1.#J	0.65	67.6	0.782	0.0224
0.04	0.410	-1.#J	-1.#J	0.70	94.2	0.805	0.0176
0.05	0.528	-1.#J	-1.#J	0.75	135.	0.830	0.0135
0.06	0.655	-1.#J	-1.#J	0.80	201.	0.858	0.0101
0.07	0.791	-1.#J	-1.#J	0.85	320.	0.892	0.00720
0.08	0.936	-1.#J	-1.#J	0.90	575.	0.934	0.00470
0.09	1.09	-1.#J	-1.#J	0.91	663.	0.945	0.00424
0.10	1.26	-1.#J	-1.#J	0.92	773.	0.956	0.00380
0.15	2.26	-1.#J	-1.#J	0.93	915.	0.969	0.00336
0.20	3.60	0.534	0.219	0.94	1.11e+003	0.983	0.00293
0.25	5.37	0.585	0.154	0.95	1.37e+003	1.00	0.00251
0.30	7.68	0.620	0.115	0.96	1.76e+003	1.02	0.00209
0.35	10.7	0.648	0.0891	0.97	2.41e+003	1.04	0.00167
0.40	14.7	0.673	0.0699	0.98	3.64e+003	1.08	0.00124
0.45	19.9	0.696	0.0555	0.99	6.98e+003	1.13	0.000773
0.50	26.9	0.718	0.0444				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0340	1	0	0.310	2	0	0.610	1	0
0.0400	2	0	0.314	1	0	0.619	1	0
0.0470	1	1	0.320	2	0	0.639	1	0
0.0490	1	0	0.321	1	0	0.640	1	0
0.0500	1	0	0.322	1	0	0.659	1	0

<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>
0.0530	1	0	0.360	1	0	0.670	1	0
0.0670	1	0	0.370	1	0	0.680	1	0
0.0710	1	0	0.375	1	0	0.690	1	0
0.0770	1	0	0.378	1	0	0.710	1	0
0.0840	1	0	0.380	1	0	0.770	1	0
0.0900	1	0	0.384	1	0	0.780	1	0
0.0990	1	0	0.390	1	0	0.825	2	0
0.100	1	0	0.400	1	0	0.837	1	0
0.108	1	0	0.419	1	0	0.850	1	0
0.110	1	0	0.420	2	0	0.888	1	0
0.124	1	0	0.428	1	0	0.890	1	0
0.145	1	0	0.444	1	0	0.930	1	0
0.150	1	0	0.446	1	0	0.950	1	0
0.162	1	0	0.460	1	0	1.01	1	0
0.170	1	0	0.461	1	0	1.02	1	1
0.179	1	0	0.466	1	0	1.05	1	0
0.181	1	0	0.470	1	0	1.13	1	0
0.200	1	0	0.480	1	0	1.19	1	0
0.201	1	0	0.490	1	0	1.27	1	0
0.202	1	0	0.500	2	0	1.31	1	0
0.210	1	0	0.503	1	0	1.32	1	1
0.220	1	0	0.520	2	0	1.34	1	1
0.228	1	0	0.522	1	0	1.42	1	0
0.230	2	0	0.530	1	0	1.57	1	0
0.231	2	0	0.538	1	0	1.84	1	0
0.240	1	0	0.543	2	0	1.87	1	0
0.250	1	0	0.561	1	0	1.98	1	0
0.269	1	0	0.564	1	0	2.16	1	1
0.270	1	0	0.570	2	0	2.25	1	0
0.278	1	0	0.580	1	0	2.41	1	0
0.297	1	0	0.598	1	0	2.49	1	1
0.300	2	0	0.600	1	0			
<b>Totals</b>							<b>122</b>	<b>6</b>

**Multipulse Study (10 Pulses) MVL - 1hr**  
C05 OD, A11 OD

ONES = 20                      ZEROES = 35                      TOTAL = 55

Percent confidence = 0.95

ED50 = 0.384 Upper FL = 1.05                      Lower FL = 0.225

Intercept = 0.661                      Slope = 1.59

Pearson's Chi-Sq = 56.2800    Probability of Chi-Sq = 0.2839

h = 1.00                      g = 0.35                      t = 1.96

Log XBAR = -0.608    Log YBAR = 4.69

SYX = 67.389 SXY = 6.976    SXX = 4.381    S0 = 28.226

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.0133	0.000190	0.0426	0.55	0.461	0.270	1.53
0.02	0.0197	0.000488	0.0552	0.60	0.555	0.319	2.27
0.03	0.0253	0.000886	0.0653	0.65	0.671	0.373	3.47
0.04	0.0306	0.00139	0.0741	0.70	0.821	0.437	5.49
0.05	0.0356	0.00199	0.0823	0.75	1.02	0.513	9.07
0.06	0.0406	0.00271	0.0901	0.80	1.30	0.611	16.0
0.07	0.0455	0.00355	0.0976	0.85	1.72	0.743	31.0
0.08	0.0504	0.00452	0.105	0.90	2.45	0.945	72.1
0.09	0.0553	0.00561	0.112	0.91	2.67	1.00	88.5
0.10	0.0603	0.00685	0.119	0.92	2.93	1.07	110.
0.15	0.0859	0.0155	0.156	0.93	3.25	1.14	141.
0.20	0.114	0.0290	0.197	0.94	3.64	1.23	185.
0.25	0.145	0.0485	0.247	0.95	4.15	1.34	253.
0.30	0.180	0.0744	0.313	0.96	4.83	1.48	366.
0.35	0.220	0.106	0.404	0.97	5.83	1.68	575.
0.40	0.267	0.143	0.539	0.98	7.49	1.97	1.05e+003
0.45	0.321	0.183	0.741	0.99	11.1	2.55	2.71e+003
0.50	0.384	0.225	1.05				

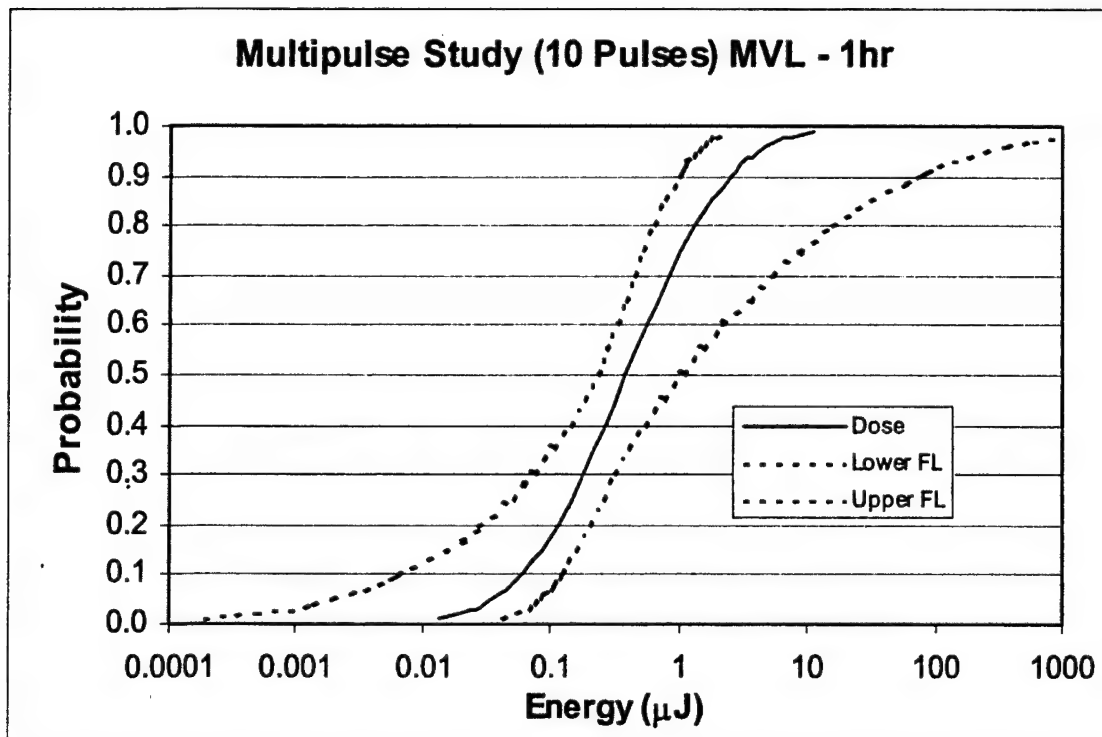
Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0350	1	0	0.133	1	0	0.340	1	0
0.0370	1	1	0.136	1	0	0.346	1	1
0.0420	1	0	0.137	1	1	0.385	1	1
0.0430	1	0	0.142	1	0	0.402	1	0
0.0460	1	0	0.162	2	1	0.425	1	0

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0510	1	0	0.194	1	0	0.459	1	1
0.0630	1	0	0.199	1	0	0.500	1	0
0.0640	1	0	0.206	1	0	0.516	1	0
0.0660	1	0	0.220	2	1	0.539	1	1
0.0680	1	0	0.240	1	1	0.572	1	1
0.0750	1	1	0.244	1	0	0.751	1	0
0.0770	1	0	0.256	1	0	1.16	1	1
0.0920	1	0	0.278	1	1	1.17	1	1
0.113	1	0	0.301	1	0	1.17	1	1
0.114	1	0	0.317	1	1	1.62	1	1
0.121	1	0	0.321	1	1	1.78	1	1
0.126	1	0	0.330	1	0	2.44	1	1
0.129	1	0	0.334	1	0			

**Totals**

**55**

**20**



**Multipulse Study (10 Pulses) MVL - 24hr**  
**C05 OD, A11 OD**

ONES = 33                ZEROES = 22                TOTAL = 55

Percent confidence = 0.95

ED50 = 0.145 Upper FL = 0.207      Lower FL = 0.0936

Intercept = 2.33                Slope = 2.78

Pearson's Chi-Sq = 52.8971      Probability of Chi-Sq = 0.4007

h = 1.00                g = 0.23                t = 1.96

Log XBAR = -0.777      Log YBAR = 5.17

SY Y = 69.443 SXY = 5.949      SXX = 2.139      S0 = 22.866

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.0212	0.00293	0.0439	0.55	0.161	0.108	0.235
0.02	0.0265	0.00450	0.0514	0.60	0.179	0.124	0.270
0.03	0.0306	0.00590	0.0569	0.65	0.200	0.141	0.316
0.04	0.0341	0.00724	0.0615	0.70	0.224	0.160	0.377
0.05	0.0372	0.00854	0.0655	0.75	0.254	0.181	0.460
0.06	0.0401	0.00982	0.0691	0.80	0.292	0.205	0.582
0.07	0.0428	0.0111	0.0725	0.85	0.343	0.235	0.772
0.08	0.0454	0.0124	0.0757	0.90	0.420	0.277	1.11
0.09	0.0479	0.0137	0.0787	0.91	0.441	0.287	1.22
0.10	0.0503	0.0150	0.0816	0.92	0.465	0.299	1.34
0.15	0.0616	0.0218	0.0951	0.93	0.493	0.313	1.49
0.20	0.0724	0.0293	0.108	0.94	0.526	0.329	1.69
0.25	0.0831	0.0375	0.121	0.95	0.567	0.348	1.94
0.30	0.0941	0.0466	0.134	0.96	0.619	0.371	2.28
0.35	0.106	0.0567	0.149	0.97	0.689	0.401	2.79
0.40	0.118	0.0679	0.165	0.98	0.796	0.445	3.66
0.45	0.131	0.0802	0.184	0.99	0.997	0.523	5.60
0.50	0.145	0.0936	0.207				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0350	1	0	0.133	1	0	0.340	1	1
0.0370	1	1	0.136	1	0	0.346	1	1
0.0420	1	0	0.137	1	0	0.385	1	1
0.0430	1	0	0.142	1	0	0.402	1	0
0.0460	1	0	0.162	2	1	0.425	1	1

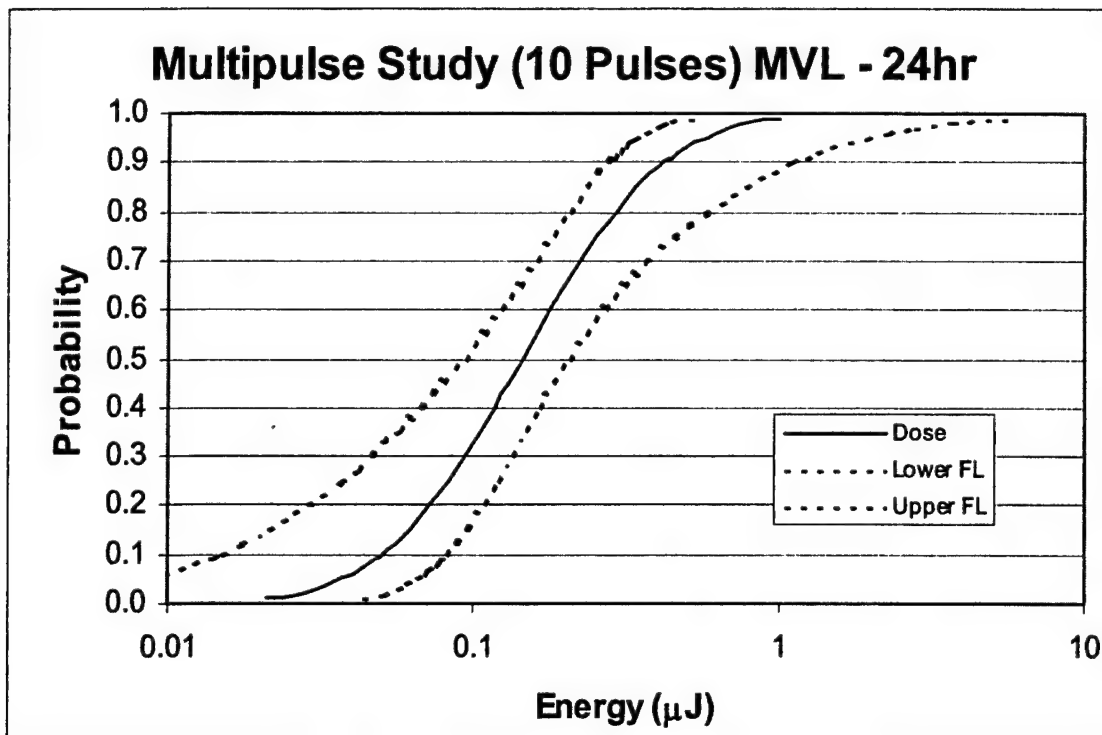


<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>
0.0510	1	0	0.194	1	1	0.459	1	1
0.0630	1	0	0.199	1	0	0.500	1	1
0.0640	1	0	0.206	1	0	0.516	1	1
0.0660	1	0	0.220	2	2	0.539	1	1
0.0680	1	0	0.240	1	1	0.572	1	1
0.0750	1	1	0.244	1	0	0.751	1	1
0.0770	1	0	0.256	1	1	1.16	1	1
0.0920	1	0	0.278	1	1	1.17	1	1
0.113	1	0	0.301	1	1	1.17	1	1
0.114	1	0	0.317	1	1	1.62	1	1
0.121	1	1	0.321	1	1	1.78	1	1
0.126	1	1	0.330	1	1	2.44	1	1
0.129	1	1	0.334	1	1			

**Totals**

**55**

**33**



**Multipulse Study (10 Pulses) FAVL - 1hr**  
C05 OD, A11 OD

ONES = 13                      ZEROES = 42                      TOTAL = 55

Percent confidence = 0.95

ED50 = 2.63    Upper FL = 8.80e-006                      Lower FL = 0.549

Intercept = -0.288    Slope = 0.686

Pearson's Chi-Sq = 54.2143    Probability of Chi-Sq = 0.3529

h = 1.00            g = 1.49            t = 1.96

Log XBAR = -0.599                      Log YBAR = 4.30

SY Y = 56.784 SXY = 3.748    SXX = 5.466    S0 = 27.851

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.00107	1.03e+010	0.0242	0.55	4.01	0.693	1.27e-006
0.02	0.00266	1.65e+008	0.0374	0.60	6.16	0.868	1.78e-007
0.03	0.00476	1.19e+007	0.0497	0.65	9.60	1.09	2.38e-008
0.04	0.00737	1.64e+006	0.0617	0.70	15.3	1.37	2.86e-009
0.05	0.0105	3.25e+005	0.0739	0.75	25.4	1.75	2.92e-010
0.06	0.0142	8.17e+004	0.0866	0.80	44.4	2.28	2.31e-011
0.07	0.0185	2.42e+004	0.0999	0.85	85.5	3.11	1.21e-012
0.08	0.0235	8.13e+003	0.114	0.90	195.	4.56	2.95e-014
0.09	0.0292	2.99e+003	0.129	0.91	238.	5.00	1.20e-014
0.10	0.0356	1.19e+003	0.146	0.92	295.	5.53	4.55e-015
0.15	0.0811	21.9	0.285	0.93	374.	6.17	1.56e-015
0.20	0.156	-1.#J	-1.#J	0.94	487.	6.97	4.72e-016
0.25	0.273	-1.#J	-1.#J	0.95	660.	8.02	1.21e-016
0.30	0.452	-1.#J	-1.#J	0.96	941.	9.44	2.44e-017
0.35	0.722	0.201	0.00448	0.97	1.46e+003	11.5	3.42e-018
0.40	1.12	0.314	0.000479	0.98	2.60e+003	15.1	2.50e-019
0.45	1.73	0.425	6.25e-005	0.99	6.50e+003	22.9	4.07e-021
0.50	2.63	0.549	8.80e-006				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0350	1	0	0.133	1	0	0.340	1	0
0.0370	1	1	0.136	1	0	0.346	1	0
0.0420	1	0	0.137	1	0	0.385	1	0
0.0430	1	0	0.142	1	0	0.402	1	0
0.0460	1	1	0.162	2	1	0.425	1	1

<b>Dose</b>	<b>Tries</b>	<b>Hits</b>	<b>Dose</b>	<b>Tries</b>	<b>Hits</b>	<b>Dose</b>	<b>Tries</b>	<b>Hits</b>
0.0510	1	0	0.194	1	0	0.459	1	0
0.0630	1	0	0.199	1	1	0.500	1	0
0.0640	1	0	0.206	1	0	0.516	1	1
0.0660	1	0	0.220	2	0	0.539	1	0
0.0680	1	0	0.240	1	1	0.572	1	0
0.0750	1	0	0.244	1	0	0.751	1	0
0.0770	1	0	0.256	1	1	1.16	1	1
0.0920	1	0	0.278	1	0	1.17	1	1
0.113	1	0	0.301	1	0	1.17	1	0
0.114	1	0	0.317	1	0	1.62	1	0
0.121	1	0	0.321	1	0	1.78	1	1
0.126	1	1	0.330	1	0	2.44	1	1
0.129	1	0	0.334	1	0			
<b>Totals</b>							<b>55</b>	<b>13</b>

**Multipulse Study (10 Pulses) FAVL - 24hr**  
**C05 OD, A11 OD**

ONES = 10                      ZEROES = 45                      TOTAL = 55

Percent confidence = 0.95

ED50 = 1.50                      Upper FL = 1.17e+003                      Lower FL = 0.589

Intercept = -0.215                      Slope = 1.22

Pearson's Chi-Sq = 60.7024                      Probability of Chi-Sq = 0.1658

h = 1.00                      g = 0.64                      t = 1.96

Log XBAR = -0.511                      Log YBAR = 4.16

SYX = 66.670                      SXY = 4.909                      SXX = 4.038                      S0 = 22.658

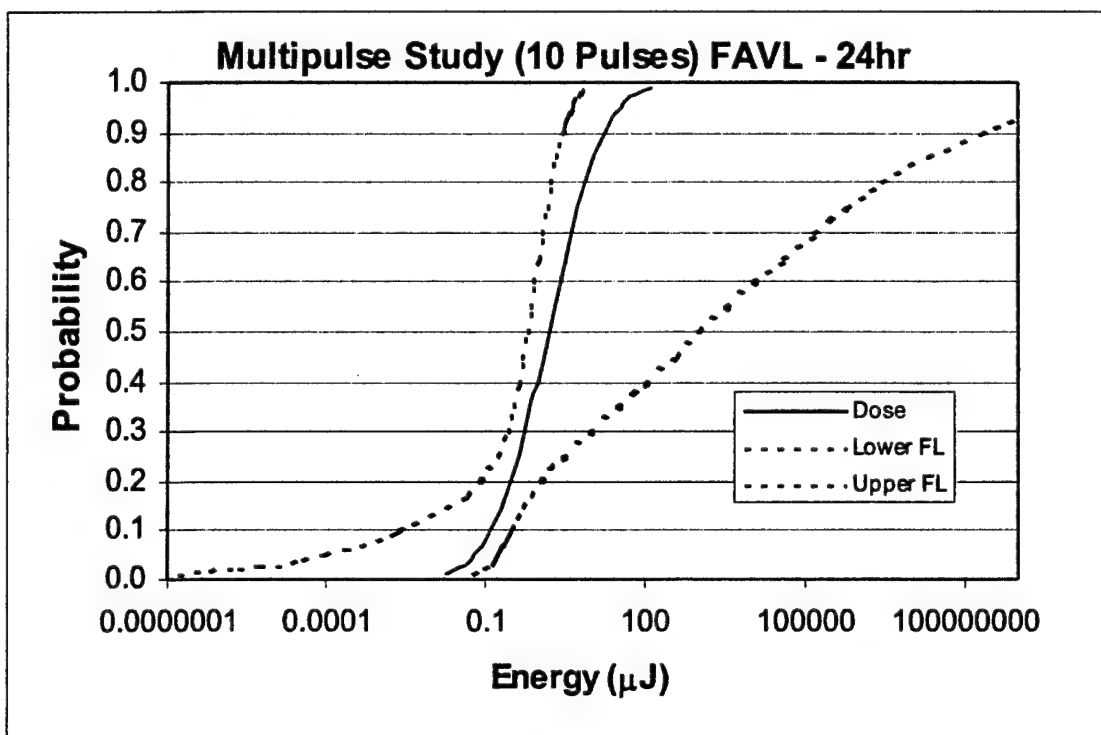
Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.0183	1.68e-007	0.0736	0.55	1.91	0.692	3.79e+003
0.02	0.0307	2.23e-006	0.101	0.60	2.43	0.809	1.26e+004
0.03	0.0426	1.14e-005	0.124	0.65	3.12	0.947	4.37e+004
0.04	0.0545	3.87e-005	0.146	0.70	4.06	1.11	1.63e+005
0.05	0.0666	0.000104	0.167	0.75	5.39	1.32	6.78e+005
0.06	0.0790	0.000240	0.189	0.85	10.7	1.98	2.12e+007
0.08	0.105	0.000946	0.236	0.90	17.0	2.60	2.20e+008
0.09	0.119	0.00169	0.261	0.91	19.0	2.77	3.86e+008
0.10	0.133	0.00286	0.290	0.92	21.5	2.97	7.14e+008
0.15	0.211	0.0222	0.506	0.93	24.6	3.21	1.40e+009
0.20	0.305	0.0808	1.10	0.94	28.5	3.50	2.98e+009
0.25	0.419	0.166	3.18	0.95	33.9	3.86	7.05e+009
0.30	0.556	0.251	10.4	0.96	41.4	4.33	1.94e+010
0.35	0.724	0.331	34.5	0.97	52.9	4.98	6.71e+010
0.40	0.929	0.412	113.	0.98	73.5	6.00	3.51e+011
0.45	1.18	0.497	364.	0.99	123.	8.04	4.75e+012
0.50	1.50	0.589	1.17e+003				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0350	1	0	0.133	1	0	0.340	1	0
0.0370	1	0	0.136	1	0	0.346	1	0
0.0420	1	0	0.137	1	0	0.385	1	0
0.0430	1	0	0.142	1	0	0.402	1	0
0.0460	1	1	0.162	2	1	0.425	1	1
0.0510	1	0	0.194	1	0	0.459	1	0

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0630	1	0	0.199	1	0	0.500	1	0
0.0640	1	0	0.206	1	0	0.516	1	1
0.0660	1	0	0.220	2	0	0.539	1	0
0.0680	1	0	0.240	1	1	0.572	1	0
0.0750	1	0	0.244	1	0	0.751	1	0
0.0770	1	0	0.256	1	1	1.16	1	1
0.0920	1	0	0.278	1	0	1.17	1	1
0.113	1	0	0.301	1	0	1.17	1	0
0.114	1	0	0.317	1	0	1.62	1	0
0.121	1	0	0.321	1	0	1.78	1	1
0.126	1	0	0.330	1	0	2.44	1	1
0.129	1	0	0.334	1	0			

**Totals**

**55 10**



**Multipulse Study (100 Pulses) MVL - 1hr**  
963 OD, A11 OS, A13 OD

ONES = 31              ZEROES = 45              TOTAL = 76

Percent confidence = 0.95

ED50 = 0.240              Upper FL = 0.366              Lower FL = 0.171

Intercept = 1.46              Slope = 2.36

Pearson's Chi-Sq = 38.8071      Probability of Chi-Sq = 0.8514

h = 1.00      g = 0.16      t = 1.96

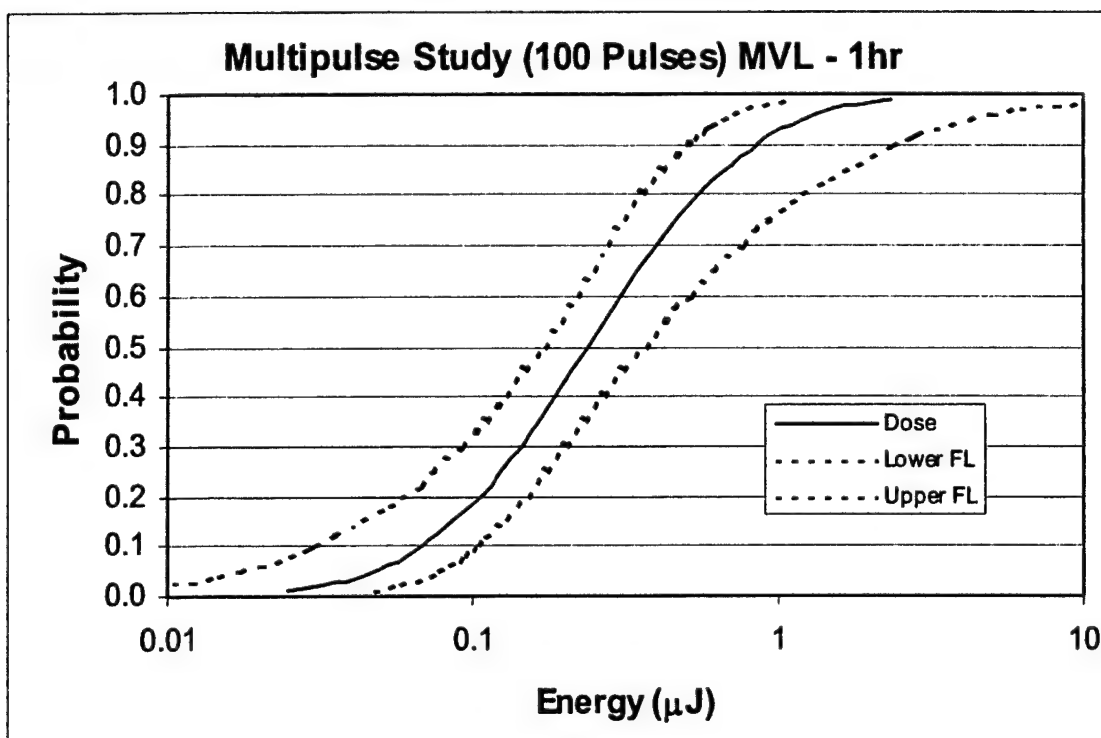
Log XBAR = -0.710      Log YBAR = 4.79

SY Y = 63.393              SXY = 10.435      SXX = 4.429      S0 = 32.106

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.0247	0.00600	0.0475	0.55	0.272	0.194	0.431
0.02	0.0323	0.00923	0.0580	0.60	0.308	0.219	0.513
0.03	0.0382	0.0121	0.0660	0.65	0.350	0.247	0.618
0.04	0.0434	0.0149	0.0727	0.70	0.401	0.278	0.756
0.05	0.0482	0.0175	0.0788	0.75	0.465	0.315	0.944
0.06	0.0526	0.0202	0.0844	0.80	0.547	0.361	1.22
0.07	0.0568	0.0228	0.0897	0.85	0.662	0.420	1.64
0.08	0.0609	0.0254	0.0947	0.90	0.841	0.507	2.40
0.09	0.0648	0.0280	0.0996	0.91	0.891	0.530	2.63
0.10	0.0687	0.0307	0.104	0.92	0.949	0.556	2.91
0.15	0.0873	0.0444	0.127	0.93	1.02	0.586	3.25
0.20	0.106	0.0591	0.150	0.94	1.10	0.621	3.68
0.25	0.124	0.0748	0.175	0.95	1.20	0.664	4.24
0.30	0.144	0.0917	0.202	0.96	1.33	0.718	5.01
0.35	0.165	0.110	0.233	0.97	1.51	0.790	6.16
0.40	0.188	0.129	0.269	0.98	1.79	0.896	8.11
0.45	0.213	0.149	0.313	0.99	2.33	1.09	12.5
0.50	0.240	0.171	0.366				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0200	2	0	0.150	2	1	0.469	1	0
0.0210	1	0	0.156	1	1	0.530	2	2
0.0300	1	0	0.160	2	1	0.540	1	1
0.0370	1	0	0.190	1	0	0.580	1	1
0.0400	4	0	0.192	1	0	0.590	1	0

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0500	3	0	0.196	1	1	0.600	1	1
0.0600	3	0	0.200	2	1	0.685	1	1
0.0690	1	0	0.236	1	0	0.810	1	1
0.0700	2	0	0.250	1	1	0.842	1	0
0.0800	3	1	0.270	1	1	0.940	1	1
0.0900	2	1	0.290	1	1	0.960	1	1
0.100	2	0	0.296	1	0	1.07	1	1
0.109	1	0	0.310	2	1	1.09	1	1
0.110	7	1	0.330	1	1	1.31	1	1
0.120	2	1	0.360	1	1	1.34	1	1
0.131	1	0	0.362	1	0	1.60	1	1
0.140	1	0	0.370	1	1	1.87	1	1
<b>Totals</b>							<b>76</b>	<b>31</b>



**Multipulse Study (100 Pulses) MVL - 24hr**  
 963 OD, A11 OS, A13 OD

ONES = 43                      ZEROES = 33                      TOTAL = 76

Percent confidence = 0.95

ED50 = 0.129 Upper FL = 0.167      Lower FL = 0.101

Intercept = 3.68              Slope = 4.14

Pearson's Chi-Sq = 20.5589      Probability of Chi-Sq = 0.9968

h = 1.00              g = 0.19              t = 1.96

Log XBAR = -0.898              Log YBAR = 4.96

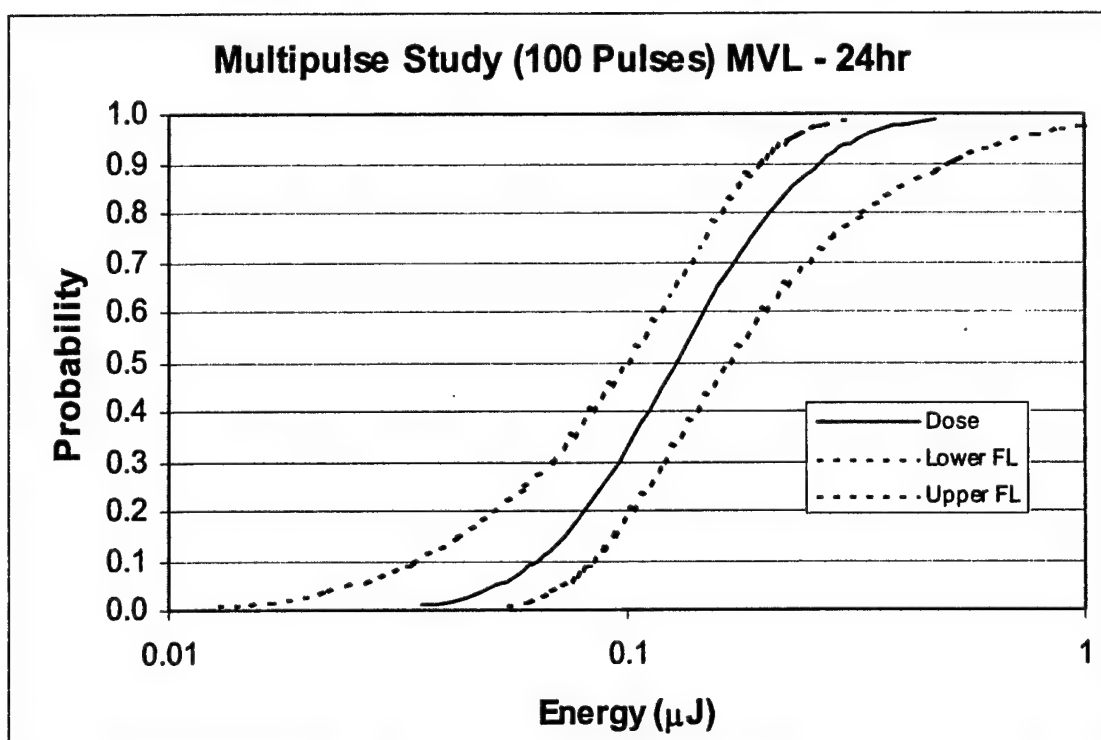
SYX = 41.051 SXY = 4.944      SXX = 1.193      S0 = 23.338

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.0355	0.0129	0.0545	0.55	0.139	0.110	0.183
0.02	0.0414	0.0167	0.0610	0.60	0.149	0.119	0.202
0.03	0.0455	0.0198	0.0655	0.65	0.160	0.128	0.224
0.04	0.0489	0.0224	0.0691	0.70	0.173	0.138	0.252
0.05	0.0519	0.0247	0.0723	0.75	0.188	0.149	0.286
0.06	0.0546	0.0269	0.0751	0.80	0.207	0.161	0.332
0.07	0.0570	0.0290	0.0776	0.85	0.230	0.176	0.397
0.08	0.0593	0.0310	0.0800	0.90	0.264	0.196	0.498
0.09	0.0615	0.0329	0.0823	0.91	0.273	0.201	0.526
0.10	0.0635	0.0348	0.0845	0.92	0.283	0.207	0.559
0.15	0.0728	0.0435	0.0943	0.93	0.294	0.213	0.597
0.20	0.0811	0.0519	0.103	0.94	0.307	0.221	0.643
0.25	0.0890	0.0600	0.112	0.95	0.323	0.229	0.700
0.30	0.0967	0.0682	0.121	0.96	0.342	0.240	0.775
0.35	0.104	0.0763	0.131	0.97	0.368	0.253	0.877
0.40	0.112	0.0846	0.142	0.98	0.405	0.271	1.03
0.45	0.121	0.0929	0.154	0.99	0.471	0.303	1.34
0.50	0.129	0.101	0.167				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0200	3	0	0.160	3	2	0.540	1	1
0.0300	1	0	0.190	2	2	0.580	1	1
0.0400	5	0	0.200	3	2	0.590	1	1
0.0500	3	0	0.240	1	1	0.600	1	1
0.0600	3	0	0.250	1	1	0.690	1	1



Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0700	3	1	0.270	1	1	0.810	1	1
0.0800	3	1	0.290	1	1	0.840	1	1
0.0900	2	1	0.300	1	1	0.940	1	1
0.100	2	0	0.310	2	1	0.960	1	1
0.110	8	1	0.330	1	1	1.07	1	1
0.120	2	2	0.360	2	2	1.09	1	1
0.130	1	1	0.370	1	1	1.31	1	1
0.140	1	0	0.470	1	1	1.34	1	1
0.150	2	2	0.530	2	2	1.60	1	1
<b>Totals</b>							<b>76</b>	<b>43</b>



**Multipulse Study (100 Pulses) FAVL - 1hr**  
**963 OD, A11 OS, A13 OD**

ONES = 6                      ZEROES = 54                      TOTAL = 60

Percent confidence = 0.95

ED50 = 0.922 Upper FL = 2.09                      Lower FL = 0.621

Intercept = 0.170                      Slope = 4.84

Pearson's Chi-Sq = 10.9224                      Probability of Chi-Sq = 0.9999

h = 1.00                      g = 0.60                      t = 1.96

Log XBAR = -0.0964                      Log YBAR = 4.70

SYX = 17.345 SXY = 1.327                      SXX = 0.274                      S0 = 7.363

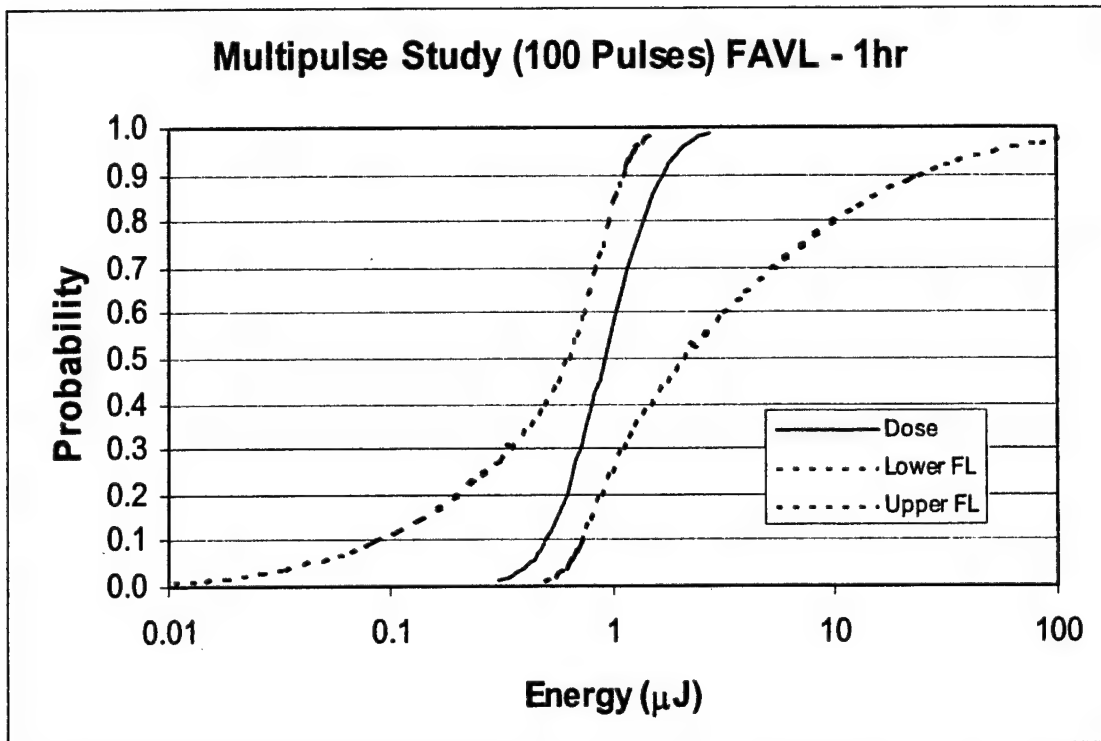
Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.305	0.0105	0.502	0.55	0.979	0.679	2.57
0.02	0.347	0.0183	0.546	0.60	1.04	0.733	3.22
0.03	0.377	0.0261	0.578	0.65	1.11	0.786	4.11
0.04	0.401	0.0340	0.603	0.70	1.18	0.838	5.35
0.05	0.422	0.0422	0.625	0.75	1.27	0.893	7.17
0.06	0.440	0.0506	0.645	0.80	1.38	0.952	9.99
0.07	0.457	0.0593	0.664	0.85	1.51	1.02	14.8
0.08	0.473	0.0682	0.681	0.90	1.70	1.11	24.3
0.09	0.487	0.0775	0.698	0.91	1.75	1.13	27.4
0.10	0.501	0.0872	0.715	0.92	1.80	1.15	31.3
0.15	0.563	0.140	0.794	0.93	1.86	1.18	36.2
0.20	0.618	0.201	0.878	0.94	1.93	1.21	42.6
0.25	0.669	0.269	0.974	0.95	2.02	1.24	51.2
0.30	0.719	0.342	1.09	0.96	2.12	1.28	63.7
0.35	0.768	0.417	1.25	0.97	2.26	1.34	83.4
0.40	0.818	0.490	1.45	0.98	2.45	1.41	119.
0.45	0.869	0.558	1.73	0.99	2.79	1.52	210.
0.50	0.922	0.621	2.09				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0200	2	0	0.150	2	0	0.580	1	0
0.0300	1	0	0.160	2	0	0.590	1	0
0.0400	4	0	0.190	1	0	0.600	1	0
0.0500	3	0	0.200	2	0	0.810	1	0
0.0600	3	0	0.250	1	0	0.940	1	0

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0700	2	0	0.270	1	0	0.960	1	1
0.0800	3	0	0.290	1	0	1.07	1	1
0.0900	2	0	0.310	2	0	1.09	1	1
0.100	2	0	0.330	1	0	1.31	1	0
0.110	7	0	0.360	1	0	1.34	1	1
0.120	2	0	0.370	1	0	1.60	1	1
0.140	1	0	0.530	2	1			

**Totals**

**60    6**



**Multipulse Study (100 Pulses) FAVL - 24hr**  
**963 OD, A11 OS, A13 OD**

ONES = 6                      ZEROES = 54                      TOTAL = 60

Percent confidence = 0.95

ED50 = 0.919 Upper FL = 1.92                      Lower FL = 0.617

Intercept = 0.196                      Slope = 5.34

Pearson's Chi-Sq = 13.7107                      Probability of Chi-Sq = 0.9988

h = 1.00                      g = 0.62                      t = 1.96

Log XBAR = -0.0811                      Log YBAR = 4.76

SYX = 19.879 SXY = 1.154                      SXX = 0.216                      S0 = 6.828

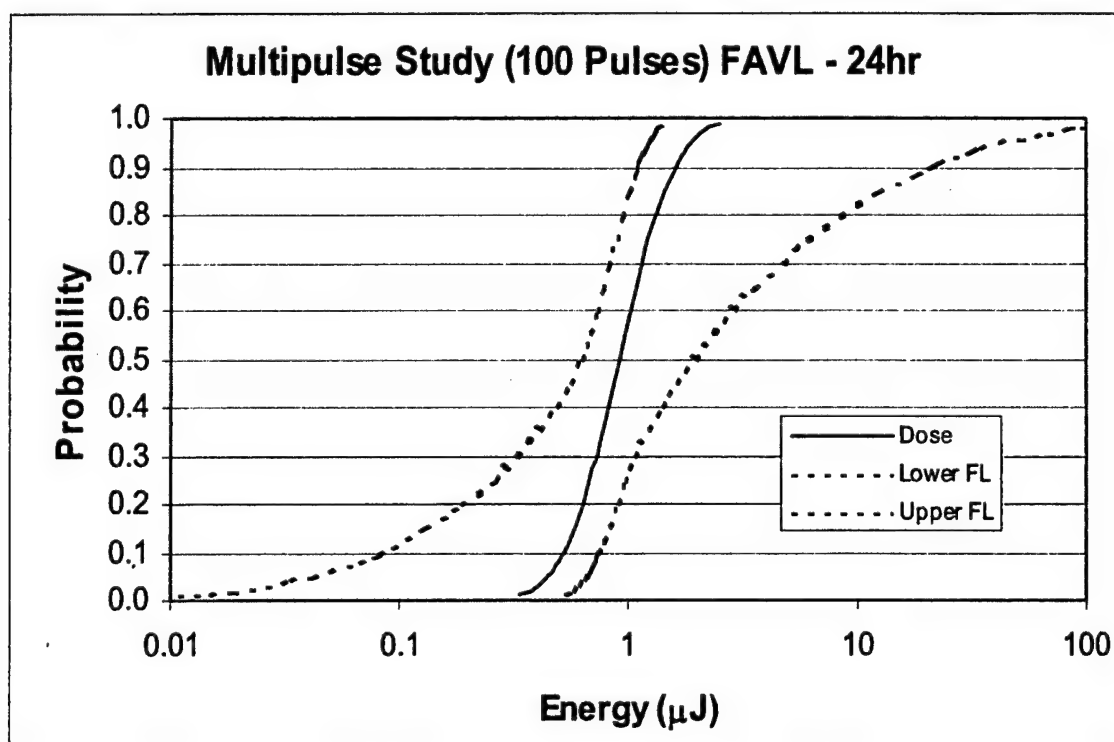
Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.337	0.0108	0.539	0.55	0.970	0.676	2.34
0.02	0.379	0.0187	0.582	0.60	1.03	0.731	2.89
0.03	0.409	0.0264	0.612	0.65	1.09	0.783	3.65
0.04	0.432	0.0342	0.636	0.70	1.15	0.834	4.71
0.05	0.452	0.0421	0.656	0.75	1.23	0.886	6.24
0.06	0.470	0.0503	0.675	0.80	1.32	0.942	8.61
0.07	0.487	0.0587	0.693	0.85	1.44	1.01	12.6
0.08	0.502	0.0674	0.709	0.90	1.60	1.08	20.4
0.09	0.516	0.0764	0.725	0.91	1.64	1.10	23.0
0.10	0.529	0.0857	0.740	0.92	1.68	1.13	26.1
0.15	0.588	0.137	0.813	0.93	1.74	1.15	30.0
0.20	0.640	0.195	0.887	0.94	1.80	1.18	35.2
0.25	0.687	0.261	0.972	0.95	1.87	1.21	42.1
0.30	0.733	0.333	1.07	0.96	1.95	1.24	52.1
0.35	0.779	0.407	1.21	0.97	2.07	1.29	67.6
0.40	0.824	0.481	1.38	0.98	2.23	1.35	95.8
0.45	0.871	0.552	1.61	0.99	2.50	1.45	166.
0.50	0.919	0.617	1.92				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0200	2	0	0.150	2	0	0.580	1	0
0.0300	1	0	0.160	2	0	0.590	1	0
0.0400	4	0	0.190	1	0	0.600	1	1
0.0500	3	0	0.200	2	0	0.810	1	0
0.0600	3	0	0.250	1	0	0.940	1	0

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0700	2	0	0.270	1	0	0.960	1	1
0.0800	3	0	0.290	1	0	1.07	1	1
0.0900	2	0	0.310	2	0	1.09	1	1
0.100	2	0	0.330	1	0	1.31	1	0
0.110	7	0	0.360	1	0	1.34	1	1
0.120	2	0	0.370	1	0	1.60	1	1
0.140	1	0	0.530	2	0			

**Totals**

**60 6**



**Multipulse Study (1,000 Pulses) MVL - 1hr**  
963 OD, A11 OS, A13 OD

ONES = 23                ZEROES = 69                TOTAL = 92

Percent confidence = 0.95

ED50 = 0.663 Upper FL = 146.                Lower FL = 0.276

Intercept = 0.181                Slope = 1.01

Pearson's Chi-Sq = 112.4487 Probability of Chi-Sq = 0.0346

h = 1.29                g = 0.61                t = 1.99

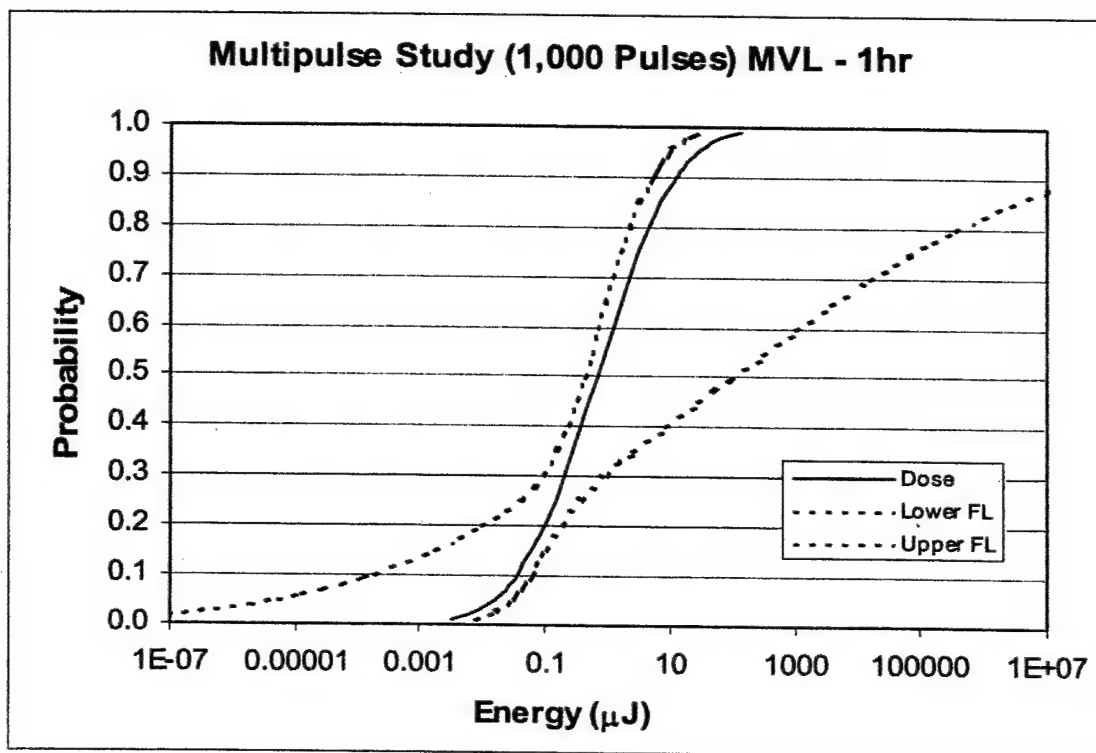
Log XBAR = -0.797                Log YBAR = 4.38

SY Y = 120.768                SXY = 8.234                SXX = 8.149                S0 = 45.535

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.00330	6.31e-009	0.00765	0.55	0.882	0.525	339.
0.02	0.00615	9.40e-008	0.0128 0.60	1.18	0.681	1.18e+003	
0.03	0.00912	5.20e-007	0.0178 0.65	1.59	0.885	4.31e+003	
0.04	0.0123	1.88e-006	0.0229 0.70	2.19	1.16	1.69e+004	
0.05	0.0156	5.32e-006	0.0282 0.75	3.08	1.55	7.46e+004	
0.06	0.0192	1.29e-005	0.0337 0.80	4.51	2.13	3.90e+005	
0.07	0.0229	2.80e-005	0.0395 0.85	7.03	3.08	2.68e+006	
0.08	0.0270	5.58e-005	0.0456 0.90	12.3	4.89	3.06e+007	
0.09	0.0312	0.000104	0.0521 0.91	14.1	5.46	5.50e+007	
0.10	0.0357	0.000185	0.0590 0.92	16.3	6.16	1.04e+008	
0.15	0.0624	0.00191	0.103 0.93	19.1	7.03	2.10e+008	
0.20	0.0973	0.0110	0.179 0.94	22.9	8.15	4.61e+008	
0.25	0.142	0.0396	0.357 0.95	28.1	9.63	1.13e+009	
0.30	0.201	0.0908	0.913 0.96	35.8	11.7	3.23e+009	
0.35	0.275	0.153	2.80 0.97	48.2	14.9	1.18e+010	
0.40	0.372	0.223	30.1 0.99	133.	34.1	9.90e+011	
0.50	0.663	0.403	100.				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.00530	1	0	0.0860	1	1	0.232	1	0
0.00940	1	1	0.0882	1	0	0.259	1	0
0.0120	1	0	0.0911	1	0	0.263	1	0
0.0170	2	0	0.0931	1	0	0.264	1	1
0.0190	1	0	0.0960	2	0	0.293	1	0

<b>Dose</b>	<b>Tries</b>	<b>Hits</b>	<b>Dose</b>	<b>Tries</b>	<b>Hits</b>	<b>Dose</b>	<b>Tries</b>	<b>Hits</b>
0.0223	1	1	0.0980	1	0	0.294	1	1
0.0236	1	0	0.103	1	0	0.297	1	1
0.0246	1	0	0.107	1	0	0.299	1	0
0.0252	1	0	0.108	1	0	0.303	1	0
0.0310	1	0	0.116	1	0	0.303	1	0
0.0315	1	0	0.131	1	0	0.335	1	0
0.0350	1	0	0.132	1	0	0.349	1	1
0.0370	1	0	0.135	1	0	0.360	1	0
0.0380	1	0	0.136	1	0	0.364	1	1
0.0420	1	0	0.138	1	0	0.365	1	0
0.0444	1	0	0.139	1	0	0.377	1	1
0.0481	1	0	0.144	1	0	0.382	1	1
0.0490	1	0	0.146	1	0	0.383	1	1
0.0531	1	0	0.148	1	0	0.384	1	1
0.0538	1	1	0.152	1	0	0.406	1	1
0.0566	1	0	0.153	1	0	0.447	1	0
0.0567	1	0	0.154	2	0	0.520	1	1
0.0593	1	0	0.162	1	0	0.551	1	0
0.0620	1	0	0.165	1	0	0.596	1	1
0.0680	1	0	0.172	1	0	0.626	1	0
0.0697	1	0	0.176	1	0	0.629	1	1
0.0700	1	1	0.182	1	1	0.662	1	0
0.0806	1	0	0.189	1	0	1.13	1	1
0.0810	1	0	0.192	1	1	1.98	1	1
0.0830	1	1	0.210	1	0			
<b>Totals</b>							<b>92</b>	<b>23</b>





**Multipulse Study (1,000 Pulses) MVL - 24hr**  
963 OD, A11 OS, A13 OD

ONES = 47                  ZEROES = 45                  TOTAL = 92

Percent confidence = 0.95

ED50 = 0.117 Upper FL = 0.179      Lower FL = 0.0744

Intercept = 1.54      Slope = 1.65

Pearson's Chi-Sq = 80.1676      Probability of Chi-Sq = 0.6848

h = 1.00      g = 0.19      t = 1.96

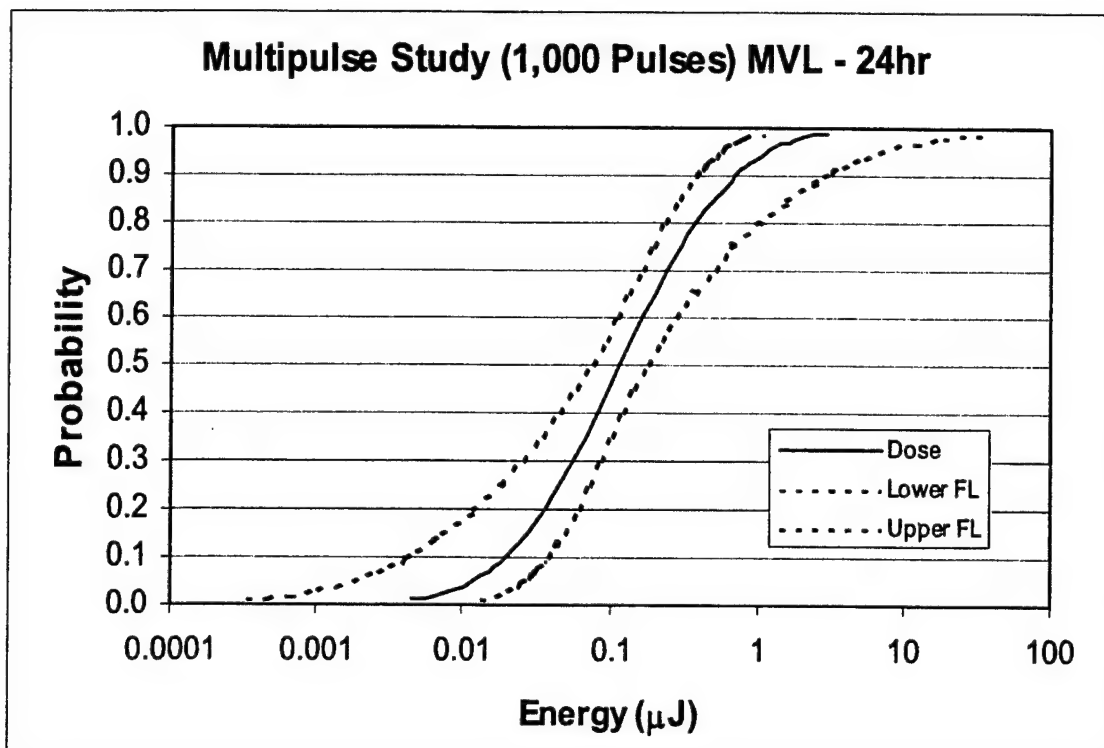
Log XBAR = -0.899                  Log YBAR = 5.05

SYX = 100.567                  SXY = 12.341 SXX = 7.466      S0 = 48.306

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.00459	0.000343	0.0132	0.55	0.140	0.0922	0.222
0.02	0.00671	0.000667	0.0173	0.60	0.167	0.112	0.282
0.03	0.00854	0.00102	0.0206	0.65	0.201	0.135	0.369
0.04	0.0102	0.00139	0.0235	0.70	0.244	0.162	0.497
0.05	0.0119	0.00180	0.0261	0.75	0.300	0.194	0.693
0.06	0.0135	0.00224	0.0286	0.80	0.379	0.235	1.02
0.07	0.0150	0.00271	0.0310	0.85	0.497	0.291	1.60
0.08	0.0166	0.00321	0.0333	0.90	0.699	0.377	2.87
0.09	0.0181	0.00375	0.0356	0.91	0.759	0.401	3.30
0.10	0.0197	0.00432	0.0378	0.92	0.831	0.429	3.85
0.15	0.0277	0.00775	0.0489	0.93	0.917	0.462	4.57
0.20	0.0363	0.0123	0.0603	0.94	1.02	0.500	5.52
0.25	0.0458	0.0181	0.0726	0.95	1.16	0.549	6.87
0.30	0.0565	0.0254	0.0865	0.96	1.34	0.611	8.87
0.35	0.0686	0.0345	0.103	0.97	1.61	0.696	12.2
0.40	0.0824	0.0457	0.122	0.98	2.05	0.829	18.5
0.45	0.0985	0.0589	0.147	0.99	3.00	1.09	35.9
0.50	0.117	0.0744	0.179				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.00530	1	0	0.0860	1	1	0.232	1	0
0.00940	1	0	0.0882	1	0	0.259	1	0
0.0120	1	0	0.0911	1	1	0.263	1	0
0.0170	2	1	0.0931	1	1	0.264	1	1
0.0190	1	0	0.0960	2	1	0.293	1	0

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0223	1	0	0.0980	1	0	0.294	1	1
0.0236	1	1	0.103	1	0	0.297	1	1
0.0246	1	0	0.107	1	0	0.299	1	1
0.0252	1	0	0.108	1	0	0.303	1	1
0.0310	1	0	0.116	1	1	0.303	1	1
0.0315	1	0	0.131	1	0	0.335	1	0
0.0350	1	0	0.132	1	0	0.349	1	1
0.0370	1	0	0.135	1	1	0.360	1	0
0.0380	1	0	0.136	1	0	0.364	1	1
0.0420	1	1	0.138	1	1	0.365	1	1
0.0444	1	0	0.139	1	0	0.377	1	1
0.0481	1	0	0.144	1	1	0.382	1	1
0.0490	1	0	0.146	1	1	0.383	1	1
0.0531	1	0	0.148	1	0	0.384	1	1
0.0538	1	0	0.152	1	0	0.406	1	1
0.0566	1	0	0.153	1	1	0.447	1	1
0.0567	1	0	0.154	2	1	0.520	1	1
0.0593	1	1	0.162	1	1	0.551	1	1
0.0620	1	1	0.165	1	1	0.596	1	1
0.0680	1	0	0.172	1	1	0.626	1	1
0.0697	1	0	0.176	1	1	0.629	1	1
0.0700	1	1	0.182	1	1	0.662	1	1
0.0806	1	0	0.189	1	0	1.13	1	1
0.0810	1	0	0.192	1	1	1.98	1	1
0.0830	1	1	0.210	1	0			
<b>Totals</b>							<b>92</b>	<b>47</b>



**Multipulse Study (1,000 Pulses) FAVL - 1hr**  
 963 OD, A11 OS, A13 OD

ONES = 12                      ZEROES = 80                      TOTAL = 92

Percent confidence = 0.95

ED50 = 1.97    Upper FL = 5.42e+004                      Lower FL = 0.593

Intercept = -0.303      Slope = 1.03

Pearson's Chi-Sq = 76.1220    Probability of Chi-Sq = 0.7912

h = 1.00              g = 0.66              t = 1.96

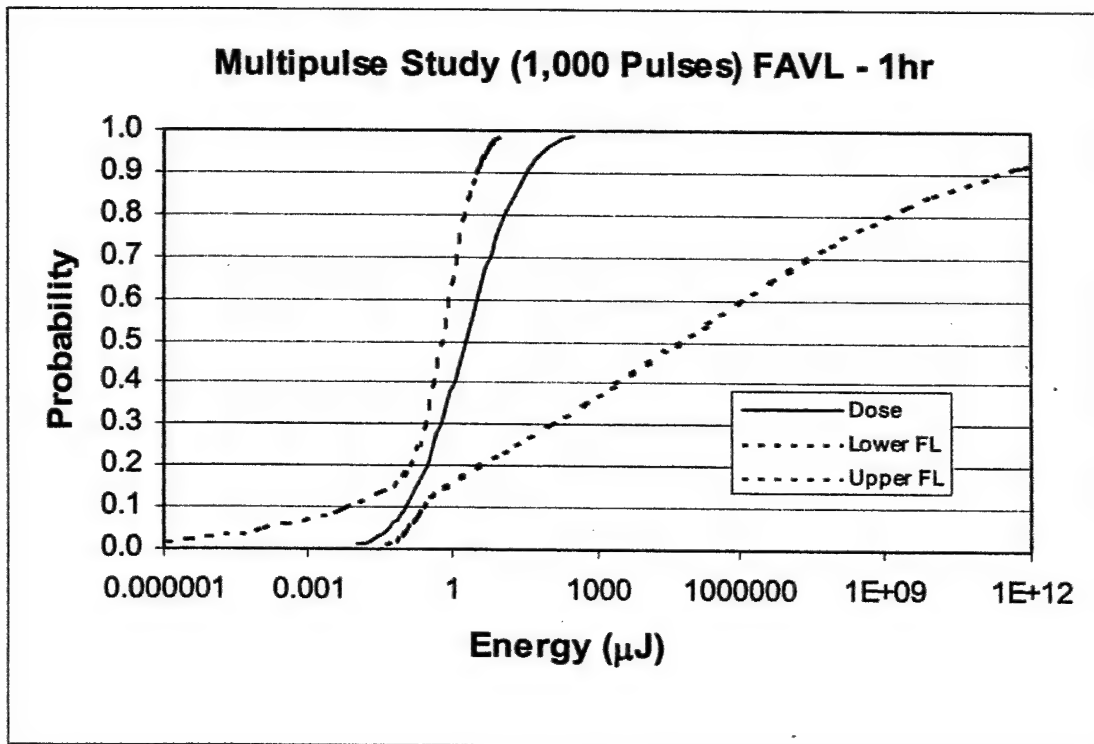
Log XBAR = -0.721              Log YBAR = 3.95

SYX = 81.952    SXY = 5.638    SXX = 5.452    S0 = 32.825

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.0111	4.64e-008	0.0448	0.55	2.60	0.703	2.36e+005
0.02	0.0203	1.13e-006	0.0647	0.60	3.46	0.834	1.05e+006
0.03	0.0298	8.45e-006	0.0826	0.65	4.64	0.991	4.96e+006
0.04	0.0399	3.81e-005	0.100	0.70	6.32	1.19	2.55e+007
0.05	0.0505	0.000128	0.118	0.75	8.82	1.44	1.49e+008
0.06	0.0617	0.000357	0.138	0.80	12.8	1.78	1.07e+009
0.07	0.0735	0.000865	0.160	0.85	19.8	2.28	1.06e+010
0.08	0.0861	0.00189	0.184	0.90	34.1	3.11	1.91e+011
0.09	0.0993	0.00376	0.214	0.91	38.9	3.35	3.83e+011
0.10	0.113	0.00695	0.251	0.92	44.9	3.63	8.18e+011
0.15	0.196	0.0560	0.763	0.93	52.5	3.97	1.89e+012
0.20	0.302	0.134	4.07	0.94	62.7	4.38	4.79e+012
0.25	0.438	0.204	23.6	0.95	76.6	4.91	1.39e+013
0.30	0.611	0.271	126.	0.96	96.9	5.60	4.84e+013
0.35	0.833	0.340	618.	0.97	129.	6.59	2.25e+014
0.40	1.12	0.415	2.84e+003	0.98	190.	8.18	1.73e+015
0.45	1.49	0.498	1.25e+004	0.99	349.	11.5	4.33e+016
0.50	1.97	0.593	5.42e+004				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.00530	1	0	0.0860	1	0	0.232	1	0
0.00940	1	0	0.0882	1	0	0.259	1	0
0.0120	1	0	0.0911	1	0	0.263	1	0
0.0170	2	0	0.0931	1	0	0.264	1	0
0.0190	1	0	0.0960	2	1	0.293	1	0

<b>Dose</b>	<b>Tries</b>	<b>Hits</b>	<b>Dose</b>	<b>Tries</b>	<b>Hits</b>	<b>Dose</b>	<b>Tries</b>	<b>Hits</b>
0.0223	1	0	0.0980	1	0	0.294	1	0
0.0236	1	0	0.103	1	0	0.297	1	0
0.0246	1	0	0.107	1	1	0.299	1	0
0.0252	1	0	0.108	1	0	0.303	1	0
0.0310	1	0	0.116	1	0	0.303	1	0
0.0315	1	0	0.131	1	0	0.335	1	0
0.0350	1	0	0.132	1	0	0.349	1	0
0.0370	1	0	0.135	1	1	0.360	1	0
0.0380	1	0	0.136	1	0	0.364	1	0
0.0420	1	0	0.138	1	0	0.365	1	0
0.0444	1	0	0.139	1	0	0.377	1	0
0.0481	1	0	0.144	1	1	0.382	1	0
0.0490	1	0	0.146	1	0	0.383	1	0
0.0531	1	0	0.148	1	0	0.384	1	0
0.0538	1	0	0.152	1	0	0.406	1	1
0.0566	1	0	0.153	1	0	0.447	1	1
0.0567	1	0	0.154	2	1	0.520	1	1
0.0593	1	1	0.162	1	0	0.551	1	0
0.0620	1	0	0.165	1	0	0.595	1	0
0.0680	1	0	0.172	1	0	0.622	1	0
0.0697	1	0	0.176	1	0	0.626	1	0
0.0700	1	0	0.182	1	0	0.629	1	0
0.0806	1	0	0.189	1	0	1.13	1	1
0.0810	1	0	0.192	1	1	1.98	1	1
0.0830	1	0	0.210	1	0			
<b>Totals</b>							<b>92</b>	<b>12</b>



**Multipulse Study (1,000 Pulses) FAVL - 24hr**  
963 OD, A11 OS, A13 OD

ONES = 8                      ZEROES = 84                      TOTAL = 92

Percent confidence = 0.95

ED50 = 3.51    Upper FL = 1.33e+016                      Lower FL = 0.783

Intercept = -0.563      Slope = 1.03

Pearson's Chi-Sq = 76.4635    Probability of Chi-Sq = 0.7830

h = 1.00          g = 0.86          t = 1.96

Log XBAR = -0.683                      Log YBAR = 3.73

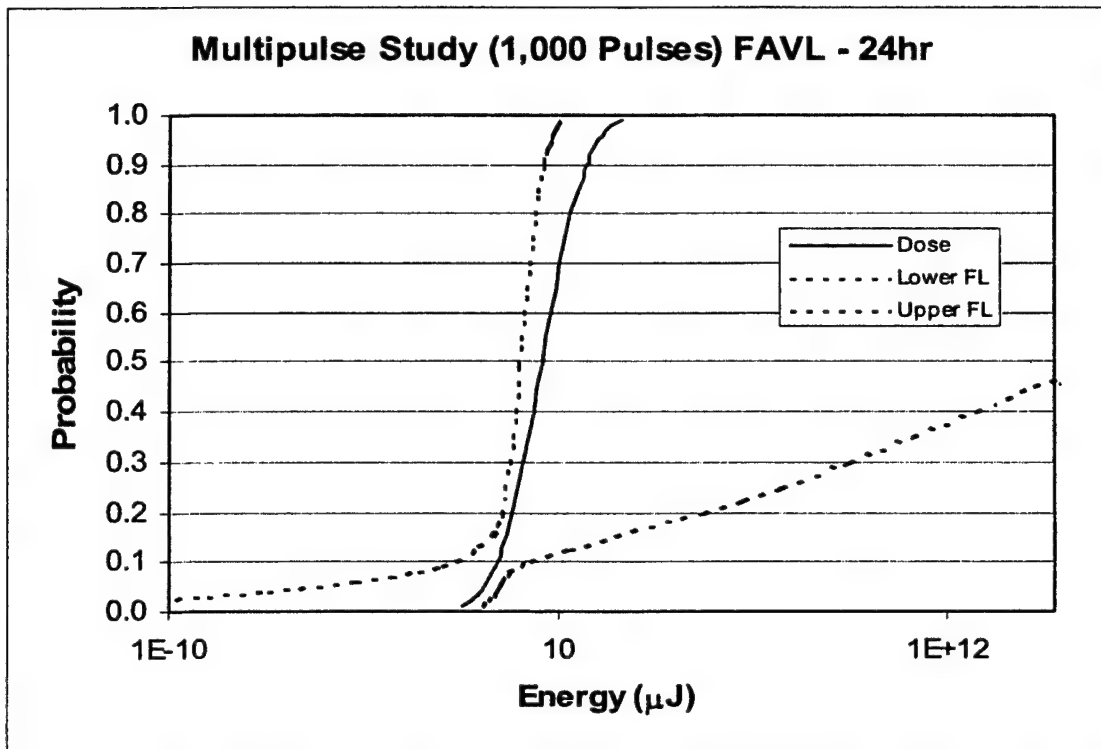
SYX = 80.937    SXY = 4.327    SXX = 4.186    S0 = 25.913

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.0197	1.94e-015	0.0723	0.55	4.64	0.917	6.01e+017
0.02	0.0362	7.25e-012	0.105	0.60	6.16	1.07	2.88e+019
0.03	0.0531	1.31e-009	0.136	0.65	8.27	1.26	1.57e+021
0.04	0.0710	6.33e-008	0.171	0.70	11.3	1.50	1.07e+023
0.05	0.0899	1.44e-006	0.212	0.75	15.8	1.79	1.02e+025
0.06	0.110	1.95e-005	0.267	0.80	22.9	2.19	1.62e+027
0.07	0.131	0.000180	0.351	0.85	35.3	2.76	6.00e+029
0.08	0.153	0.00117	0.501	0.90	60.9	3.69	1.02e+033
0.09	0.177	0.00542	0.824	0.91	69.5	3.96	6.18e+033
0.10	0.202	0.0172	1.68	0.92	80.2	4.28	4.35e+034
0.15	0.349	0.136	486.	0.93	93.9	4.65	3.73e+035
0.20	0.538	0.227	1.35e+005	0.94	112.	5.10	4.10e+036
0.25	0.781	0.307	1.95e+007	0.95	137.	5.67	6.33e+037
0.30	1.09	0.388	1.76e+009	0.96	173.	6.42	1.57e+039
0.35	1.49	0.472	1.16e+011	0.97	231.	7.49	8.19e+040
0.40	1.99	0.564	6.26e+012	0.98	340.	9.17	1.57e+043
0.45	2.65	0.667	2.98e+014	0.99	624.	12.6	6.18e+046
0.50	3.51	0.783	1.33e+016				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.00530	1	0	0.0860	1	0	0.232	1	0
0.00940	1	0	0.0882	1	0	0.259	1	0
0.0120	1	0	0.0911	1	0	0.263	1	0
0.0170	2	0	0.0931	1	1	0.264	1	0
0.0190	1	0	0.0960	2	1	0.293	1	0

<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>
0.0223	1	0	0.0980	1	0	0.294	1	0
0.0236	1	0	0.103	1	0	0.297	1	0
0.0246	1	0	0.107	1	0	0.299	1	0
0.0252	1	0	0.108	1	0	0.303	1	0
0.0310	1	0	0.116	1	0	0.303	1	0
0.0315	1	0	0.131	1	0	0.335	1	0
0.0350	1	0	0.132	1	0	0.349	1	0
0.0370	1	0	0.135	1	1	0.360	1	0
0.0380	1	0	0.136	1	0	0.364	1	0
0.0420	1	0	0.138	1	0	0.365	1	0
0.0444	1	0	0.139	1	0	0.377	1	0
0.0481	1	0	0.144	1	1	0.382	1	0
0.0490	1	0	0.146	1	0	0.383	1	0
0.0531	1	0	0.148	1	0	0.384	1	0
0.0538	1	0	0.152	1	0	0.406	1	0
0.0566	1	0	0.153	1	0	0.447	1	0
0.0567	1	0	0.154	2	0	0.520	1	1
0.0593	1	0	0.162	1	0	0.551	1	0
0.0620	1	0	0.165	1	0	0.596	1	0
0.0680	1	0	0.172	1	0	0.626	1	0
0.0697	1	0	0.176	1	0	0.629	1	0
0.0700	1	0	0.182	1	0	0.662	1	0
0.0806	1	0	0.189	1	0	1.13	1	1
0.0810	1	0	0.192	1	1	1.98	1	1
0.0830	1	0	0.210	1	0			
<b>Totals</b>							<b>92</b>	<b>8</b>





**Multipulse Study (10,000 Pulses) MVL - 1hr**  
**C15 OD, C15 OS**

ONES =14                      ZEROES = 35 TOTAL = 49

Percent confidence = 0.95

ED50 = 0.225 Upper FL = 0.382      Lower FL = 0.160

Intercept = 2.06              Slope = 3.18

Pearson's Chi-Sq = 53.4059      Probability of Chi-Sq = 0.2110

h = 1.00              g = 0.26              t = 1.96

Log XBAR = -0.764      Log YBAR = 4.63

SYX = 68.150 SXY = 4.643      SXX = 1.462      S0 = 17.725

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.0417	0.00881	0.0726	0.55	0.247	0.176	0.446
0.02	0.0508	0.0130	0.0837	0.60	0.271	0.192	0.524
0.03	0.0576	0.0167	0.0917	0.65	0.298	0.209	0.623
0.04	0.0633	0.0201	0.0984	0.70	0.329	0.228	0.751
0.05	0.0683	0.0233	0.104	0.75	0.367	0.249	0.923
0.06	0.0729	0.0265	0.110	0.80	0.414	0.274	1.16
0.07	0.0772	0.0296	0.115	0.85	0.477	0.305	1.53
0.08	0.0813	0.0326	0.120	0.90	0.570	0.348	2.17
0.09	0.0852	0.0356	0.124	0.91	0.595	0.359	2.37
0.10	0.0889	0.0386	0.129	0.92	0.624	0.371	2.59
0.15	0.106	0.0535	0.150	0.93	0.656	0.385	2.87
0.20	0.122	0.0686	0.171	0.94	0.695	0.402	3.22
0.25	0.138	0.0839	0.195	0.95	0.742	0.421	3.67
0.30	0.154	0.0992	0.221	0.96	0.801	0.444	4.27
0.35	0.170	0.115	0.251	0.97	0.880	0.474	5.16
0.40	0.187	0.130	0.287	0.98	0.998	0.518	6.64
0.45	0.206	0.145	0.330	0.99	1.22	0.594	9.88
0.50	0.225	0.160	0.382				

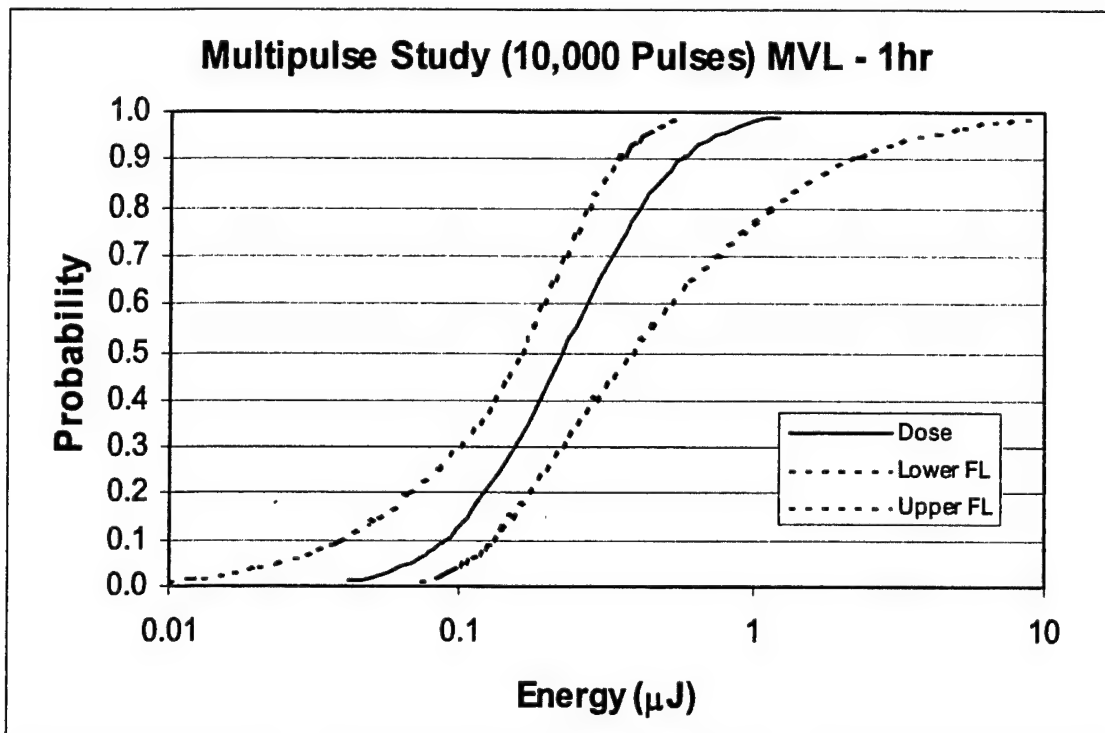
Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0167	1	0	0.0730	1	0	0.179	1	0
0.0219	1	0	0.0740	1	0	0.189	1	0
0.0229	1	0	0.0851	1	0	0.191	1	1
0.0290	1	0	0.0905	1	0	0.194	1	0
0.0360	1	0	0.0930	1	0	0.212	1	0

<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>
0.0420	1	0	0.0992	1	0	0.215	1	1
0.0440	1	0	0.104	1	0	0.219	1	0
0.0481	1	0	0.108	1	0	0.326	2	2
0.0510	1	0	0.112	1	0	0.354	1	0
0.0571	1	0	0.116	1	0	0.432	1	1
0.0580	1	0	0.118	1	0	0.450	1	1
0.0582	1	0	0.122	1	0	0.452	1	1
0.0686	1	1	0.127	1	0	0.463	1	1
0.0690	1	1	0.150	1	0	0.580	1	1
0.0720	1	0	0.168	1	0	0.606	1	1
0.0722	1	0	0.175	1	1	0.628	1	1

**Totals**

**49**

**14**



**Multipulse Study (10,000 Pulses) MVL - 24hr**  
**C15 OD, C15 OS**

ONES = 26                  ZEROES = 23                  TOTAL = 49

Percent confidence = 0.95

ED50 = 0.106 Upper FL = 0.141      Lower FL = 0.0805

Intercept = 4.59      Slope = 4.71

Pearson's Chi-Sq = 38.9457      Probability of Chi-Sq = 0.7600

h = 1.00      g = 0.27      t = 1.96

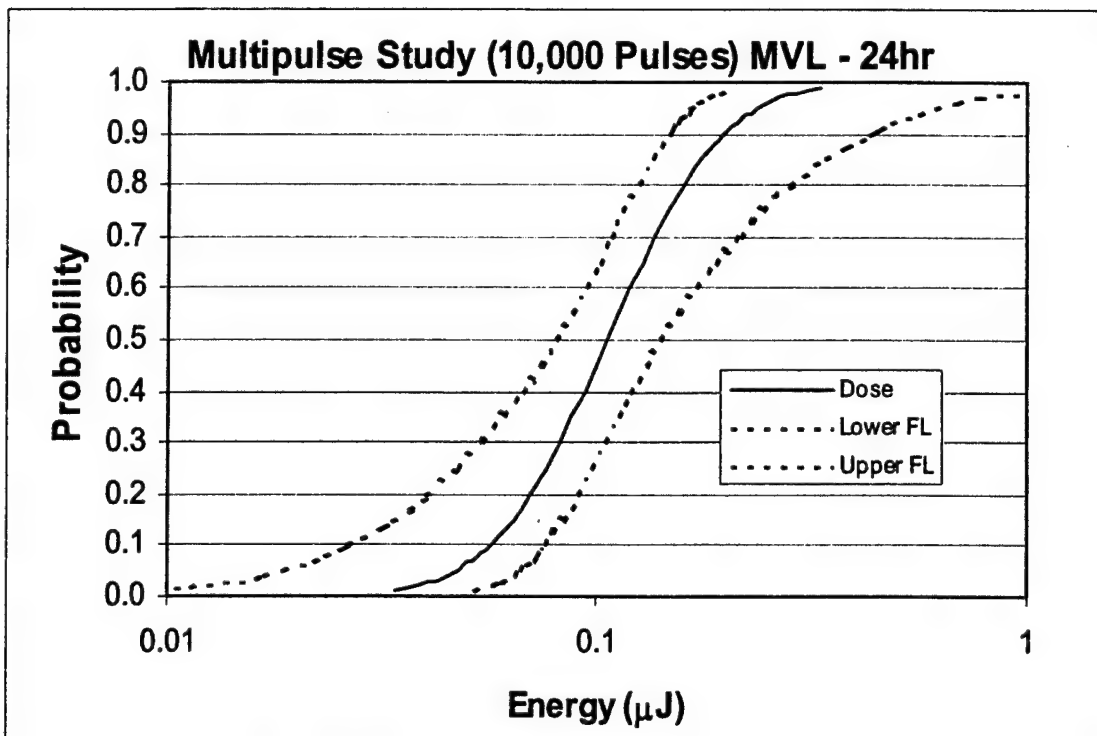
Log XBAR = -0.981      Log YBAR = 4.97

SY Y = 53.026 SXY = 2.988      SXX = 0.634      S0 = 15.958

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.0340	0.00952	0.0524	0.55	0.113	0.0872	0.155
0.02	0.0389	0.0125	0.0576	0.60	0.120	0.0938	0.170
0.03	0.0423	0.0149	0.0611	0.65	0.128	0.101	0.190
0.04	0.0451	0.0169	0.0640	0.70	0.137	0.108	0.214
0.05	0.0475	0.0188	0.0665	0.75	0.147	0.115	0.244
0.06	0.0496	0.0205	0.0687	0.80	0.160	0.124	0.285
0.07	0.0516	0.0222	0.0707	0.85	0.176	0.134	0.342
0.08	0.0534	0.0237	0.0725	0.90	0.198	0.147	0.433
0.09	0.0551	0.0253	0.0743	0.91	0.204	0.150	0.459
0.10	0.0567	0.0268	0.0759	0.92	0.211	0.154	0.488
0.15	0.0639	0.0339	0.0835	0.93	0.218	0.158	0.523
0.20	0.0703	0.0406	0.0904	0.94	0.227	0.163	0.566
0.25	0.0763	0.0473	0.0972	0.95	0.237	0.168	0.618
0.30	0.0821	0.0539	0.104	0.96	0.249	0.174	0.687
0.35	0.0879	0.0606	0.112	0.97	0.266	0.182	0.781
0.40	0.0937	0.0672	0.120	0.98	0.289	0.194	0.929
0.45	0.0997	0.0739	0.130	0.99	0.331	0.212	1.22
0.50	0.106	0.0805	0.141				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0167	1	0	0.0730	1	0	0.179	1	1
0.0219	1	0	0.0740	1	0	0.189	1	1
0.0229	1	0	0.0851	1	0	0.191	1	1
0.0290	1	0	0.0905	1	0	0.194	1	1
0.0360	1	0	0.0930	1	0	0.212	1	1

<b>Dose</b>	<b>Tries</b>	<b>Hits</b>	<b>Dose</b>	<b>Tries</b>	<b>Hits</b>	<b>Dose</b>	<b>Tries</b>	<b>Hits</b>
0.0420	1	0	0.0992	1	0	0.215	1	1
0.0440	1	0	0.104	1	0	0.219	1	0
0.0481	1	0	0.108	1	1	0.326	2	2
0.0510	1	0	0.112	1	1	0.354	1	1
0.0571	1	1	0.116	1	1	0.432	1	1
0.0580	1	0	0.118	1	1	0.450	1	1
0.0582	1	0	0.122	1	1	0.452	1	1
0.0686	1	0	0.127	1	0	0.463	1	1
0.0690	1	1	0.150	1	1	0.580	1	1
0.0720	1	0	0.168	1	1	0.606	1	1
0.0722	1	0	0.175	1	1	0.628	1	1
<b>Totals</b>							<b>49</b>	<b>26</b>



**Multipulse Study (10,000 Pulses) FAVL - 1hr**  
**C15 OD, C15 OS**

ONES = 11                      ZEROES = 38                      TOTAL = 49

Percent confidence = 0.95

ED50 = 0.355                      Upper FL = 1.48                      Lower FL = 0.216

Intercept = 0.954                      Slope = 2.12

Pearson's Chi-Sq = 38.1538                      Probability of Chi-Sq = 0.7879

h = 1.00                      g = 0.40                      t = 1.96

Log XBAR = -0.746                      Log YBAR = 4.37

SYX = 47.661                      SXY = 4.476                      SXX = 2.107                      S0 = 19.371

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.0285	0.00105	0.0643	0.55	0.407	0.242	2.08
0.02	0.0384	0.00232	0.0783	0.60	0.468	0.270	2.97
0.03	0.0463	0.00382	0.0892	0.65	0.540	0.301	4.32
0.04	0.0533	0.00555	0.0985	0.70	0.628	0.336	6.42
0.05	0.0597	0.00751	0.107	0.75	0.738	0.376	9.89
0.06	0.0659	0.00969	0.115	0.80	0.885	0.426	16.0
0.07	0.0718	0.0121	0.123	0.85	1.09	0.491	28.3
0.08	0.0775	0.0147	0.131	0.90	1.43	0.584	58.0
0.09	0.0831	0.0176	0.138	0.91	1.52	0.609	69.0
0.10	0.0886	0.0206	0.146	0.92	1.63	0.637	83.3
0.15	0.116	0.0393	0.187	0.93	1.76	0.670	103
0.20	0.143	0.0625	0.239	0.94	1.92	0.707	129
0.25	0.171	0.0885	0.310	0.95	2.11	0.753	169
0.30	0.201	0.115	0.412	0.96	2.37	0.810	230
0.35	0.234	0.141	0.557	0.97	2.73	0.887	338
0.40	0.270	0.166	0.765	0.98	3.29	0.998	563
0.45	0.310	0.191	1.06	0.99	4.43	1.20	1.26e+003
0.50	0.355	0.216	1.48				

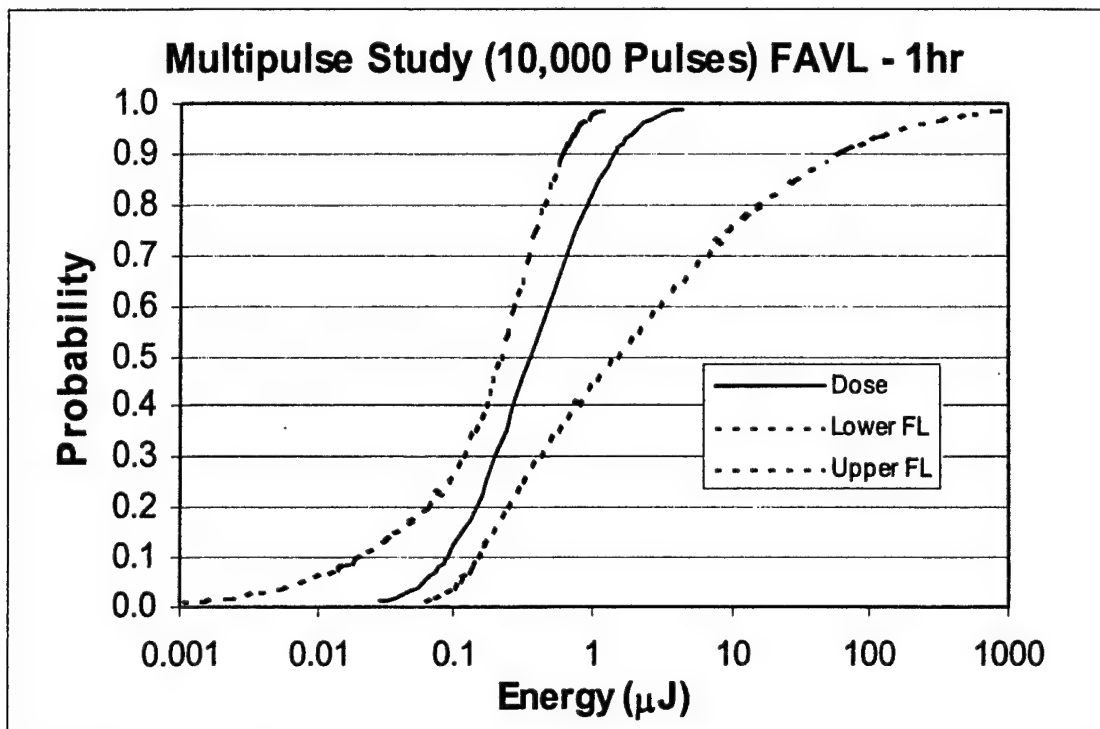
Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0167	1	0	0.0730	1	0	0.179	1	0
0.0219	1	0	0.0740	1	0	0.189	1	0
0.0229	1	0	0.0851	1	0	0.191	1	0
0.0290	1	0	0.0905	1	0	0.194	1	1
0.0360	1	0	0.0930	1	0	0.212	1	0

<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>
0.0420	1	0	0.0992	1	0	0.215	1	0
0.0440	1	0	0.104	1	0	0.219	1	1
0.0481	1	0	0.108	1	0	0.326	2	2
0.0510	1	0	0.112	1	1	0.354	1	1
0.0571	1	0	0.116	1	1	0.432	1	0
0.0580	1	0	0.118	1	0	0.450	1	0
0.0582	1	0	0.122	1	0	0.452	1	1
0.0686	1	0	0.127	1	1	0.463	1	1
0.0690	1	0	0.150	1	0	0.580	1	0
0.0720	1	0	0.168	1	0	0.606	1	1
0.0722	1	0	0.175	1	0	0.628	1	0

**Totals**

**49**

**11**



**Multipulse Study (10,000 Pulses) FAVL - 24hr**  
**C15 OD, C15 OS**

ONES = 4                      ZEROES = 45                      TOTAL = 49

Percent confidence = 0.95

ED50 = 0.586 Upper FL = 25.2      Lower FL = 0.375

Intercept = 0.840      Slope = 3.61

Pearson's Chi-Sq = 12.0649      Probability of Chi-Sq = 1.0000

h = 1.00      g = 0.76      t = 1.96

Log XBAR = -0.459      Log YBAR = 4.18

SYX = 17.117 SXY = 1.398      SXX = 0.387      S0 = 8.050

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	0.133	0.000171	0.233	0.55	0.634	0.401	46.0
0.02	0.158	0.000649	0.262	0.60	0.688	0.427	85.2
0.03	0.177	0.00150	0.284	0.65	0.749	0.454	162.
0.04	0.192	0.00282	0.303	0.70	0.818	0.483	319.
0.05	0.205	0.00467	0.321	0.75	0.900	0.515	665.
0.06	0.217	0.00716	0.338	0.80	1.00	0.551	1.51e+003
0.07	0.229	0.0104	0.355	0.85	1.13	0.595	3.95e+003
0.08	0.239	0.0144	0.373	0.90	1.33	0.654	1.32e+004
0.09	0.249	0.0193	0.392	0.91	1.38	0.669	1.77e+004
0.10	0.259	0.0251	0.412	0.92	1.43	0.685	2.44e+004
0.15	0.302	0.0697	0.547	0.93	1.50	0.704	3.46e+004
0.20	0.342	0.133	0.807	0.94	1.58	0.724	5.11e+004
0.25	0.381	0.196	1.34	0.95	1.67	0.749	7.98e+004
0.30	0.419	0.246	2.36	0.96	1.79	0.779	1.35e+005
0.35	0.458	0.286	4.26	0.97	1.94	0.817	2.57e+005
0.40	0.498	0.319	7.71	0.98	2.17	0.869	6.06e+005
0.45	0.540	0.348	13.9	0.99	2.58	0.959	2.34e+006
0.50	0.586	0.375	25.2				

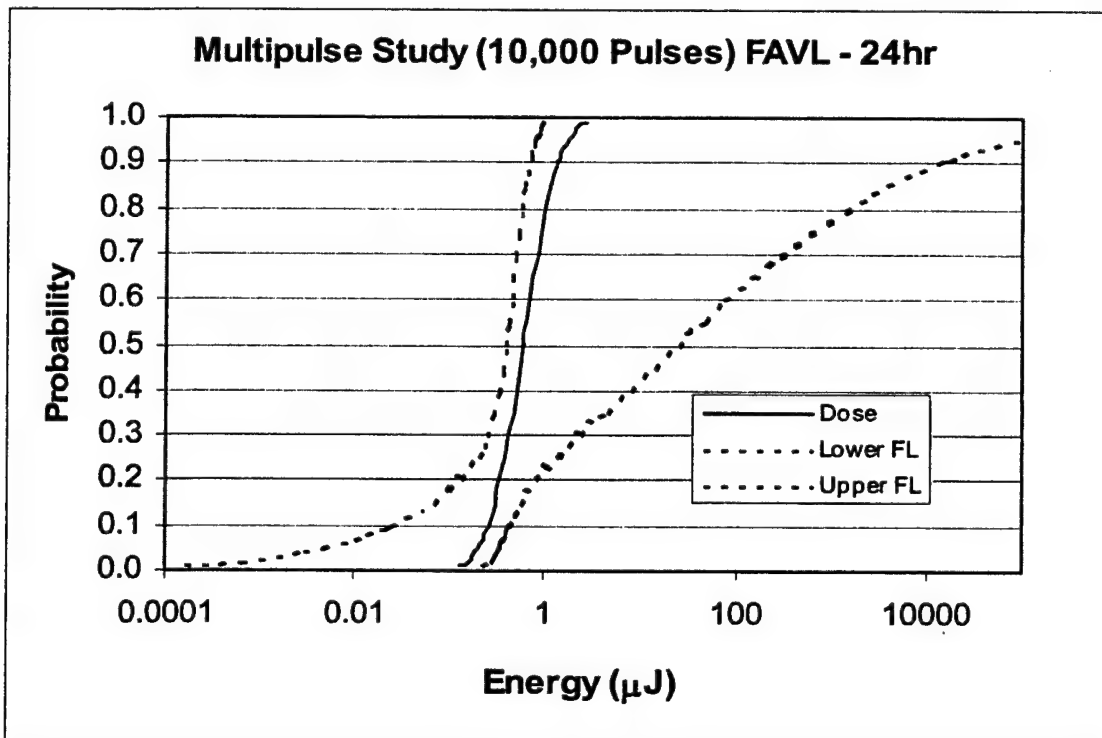
Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0167	1	0	0.0730	1	0	0.179	1	0
0.0219	1	0	0.0740	1	0	0.189	1	0
0.0229	1	0	0.0851	1	0	0.191	1	0
0.0290	1	0	0.0905	1	0	0.194	1	0
0.0360	1	0	0.0930	1	0	0.212	1	0



Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.0420	1	0	0.0992	1	0	0.215	1	0
0.0440	1	0	0.104	1	0	0.219	1	0
0.0481	1	0	0.108	1	0	0.326	2	1
0.0510	1	0	0.112	1	0	0.354	1	1
0.0571	1	0	0.116	1	0	0.432	1	0
0.0580	1	0	0.118	1	0	0.450	1	0
0.0582	1	0	0.122	1	0	0.452	1	1
0.0686	1	0	0.127	1	0	0.463	1	0
0.0690	1	0	0.150	1	0	0.580	1	0
0.0720	1	0	0.168	1	0	0.606	1	1
0.0722	1	0	0.175	1	0	0.628	1	0

**Totals**

**49 4**



**Modelocked/CW Study (ML) MVL - 24hr**  
**A13 OS, A39 OS, C03 OS, C91 OD, C63 OD**

ONES = 32                      ZEROES = 43                      TOTAL = 75

Percent confidence = 0.95

ED50 = 5.90    Upper FL = 6.60                      Lower FL = 5.23

Intercept = -6.05                      Slope = 7.85

Pearson's Chi-Sq = 43.0049    Probability of Chi-Sq = 0.8799

h = 1.00                      g = 0.19                      t = 1.96

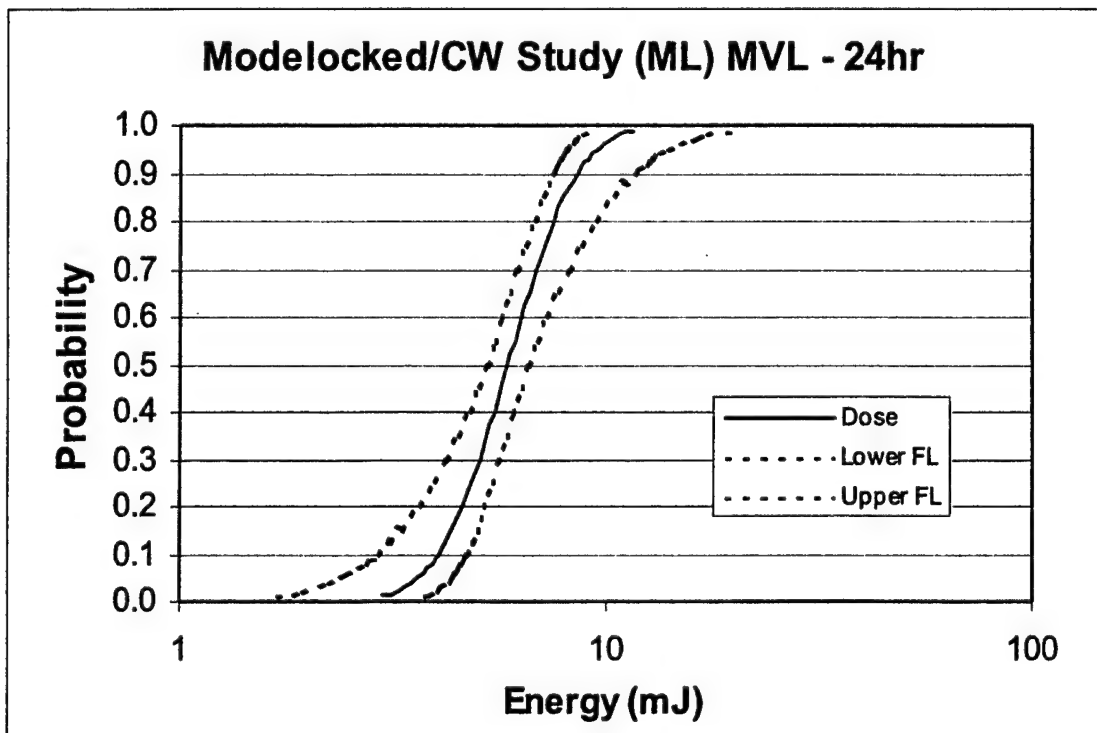
Log XBAR = 0.778                      Log YBAR = 5.05

SYX = 63.077    SXY = 2.555    SXX = 0.325    S0 = 30.450

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	2.98	1.70	3.75	0.55	6.12	5.48	6.91
0.02	3.23	1.96	3.98	0.60	6.35	5.71	7.26
0.03	3.40	2.14	4.13	0.65	6.61	5.95	7.67
0.04	3.53	2.29	4.24	0.70	6.88	6.19	8.16
0.05	3.64	2.41	4.34	0.75	7.19	6.45	8.74
0.06	3.74	2.53	4.43	0.80	7.55	6.73	9.45
0.07	3.83	2.63	4.50	0.85	7.99	7.05	10.4
0.08	3.91	2.73	4.58	0.90	8.59	7.46	11.7
0.09	3.98	2.82	4.64	0.91	8.74	7.56	12.1
0.10	4.05	2.90	4.70	0.92	8.91	7.67	12.5
0.15	4.35	3.28	4.97	0.93	9.09	7.79	12.9
0.20	4.61	3.61	5.20	0.94	9.31	7.93	13.5
0.25	4.84	3.91	5.42	0.95	9.56	8.08	14.1
0.30	5.06	4.19	5.63	0.96	9.86	8.27	14.9
0.35	5.27	4.46	5.85	0.97	10.2	8.51	15.9
0.40	5.48	4.73	6.08	0.98	10.8	8.83	17.3
0.45	5.69	4.98	6.33	0.99	11.7	9.36	19.9
0.50	5.90	5.23	6.60				

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.120	1	0	4.72	1	0	6.81	1	0
0.370	1	0	4.89	1	1	7.02	1	0
0.570	1	0	5.31	1	0	7.22	2	1
0.720	1	0	5.39	1	0	7.27	3	2
0.830	1	0	5.49	2	1	7.36	1	1

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
1.53	1	0	5.51	1	0	7.40	1	1
1.74	1	0	5.52	1	0	7.43	2	2
1.80	1	0	5.53	1	0	7.46	1	1
2.55	1	0	5.54	1	1	7.47	1	0
2.78	1	0	5.55	2	2	7.48	1	1
3.11	1	0	5.58	2	0	7.50	3	3
3.65	1	0	6.07	1	1	7.53	1	1
3.69	1	0	6.11	1	0	7.62	2	2
3.78	5	0	6.19	1	1	7.74	1	1
3.84	3	0	6.20	1	0	7.97	1	1
3.85	3	1	6.40	1	0	8.20	1	1
3.99	1	0	6.47	1	1	8.63	1	1
4.08	1	0	6.52	1	1	9.27	1	1
4.47	1	1	6.64	1	0	14.4	1	1
<b>Totals</b>							<b>75</b>	<b>32</b>



**Modelocked/CW Study (ML) FAVL - 24hr**  
**A13 OS, A39 OS, C03 OS, C91 OD, C63 OD**

ONES = 24                  ZEROES = 51                  TOTAL = 75

Percent confidence = 0.95

ED50 = 6.71    Upper FL = 7.47    Lower FL = 6.12

Intercept = -8.51    Slope = 10.3

Pearson's Chi-Sq = 30.9930    Probability of Chi-Sq = 0.9963

h = 1.00    g = 0.25    t = 1.96

Log XBAR = 0.818    Log YBAR = 4.91

SY Y = 46.388 SXY = 1.496    SXX = 0.145    S0 = 26.213

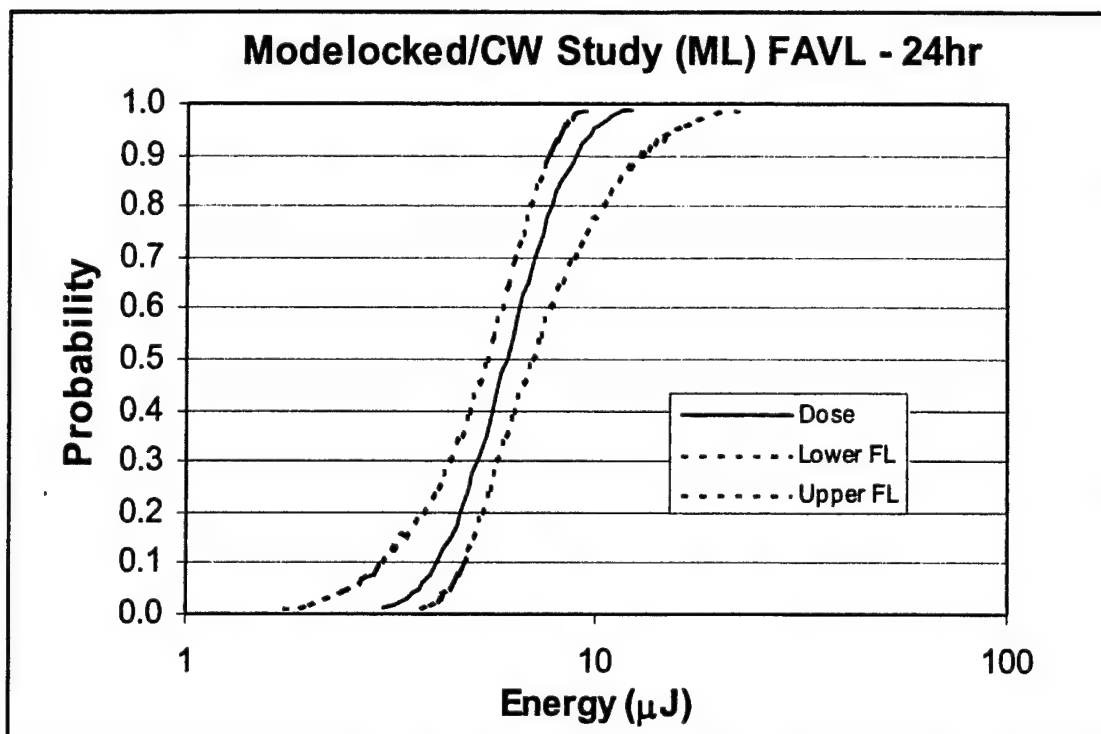
<u>Prob</u>	<u>Dose</u>	<u>LFL</u>	<u>UFL</u>	<u>Prob</u>	<u>Dose</u>	<u>LFL</u>	<u>UFL</u>
0.01	3.99	2.39	4.78	0.55	6.90	6.32	7.78
0.02	4.24	2.69	4.99	0.60	7.10	6.52	8.15
0.03	4.41	2.90	5.13	0.65	7.32	6.71	8.56
0.04	4.54	3.07	5.23	0.70	7.55	6.90	9.04
0.05	4.64	3.22	5.32	0.75	7.80	7.10	9.61
0.06	4.74	3.35	5.40	0.80	8.10	7.32	10.3
0.07	4.82	3.46	5.47	0.85	8.46	7.57	11.2
0.08	4.90	3.57	5.53	0.90	8.94	7.89	12.4
0.09	4.97	3.67	5.59	0.91	9.06	7.97	12.7
0.10	5.04	3.76	5.65	0.92	9.19	8.05	13.1
0.15	5.32	4.18	5.89	0.93	9.34	8.14	13.5
0.20	5.56	4.53	6.10	0.94	9.50	8.25	14.0
0.25	5.77	4.84	6.30	0.95	9.70	8.37	14.6
0.30	5.97	5.14	6.50	0.96	9.93	8.51	15.2
0.35	6.16	5.41	6.71	0.97	10.2	8.68	16.1
0.40	6.34	5.66	6.94	0.98	10.6	8.92	17.4
0.45	6.53	5.89	7.19	0.99	11.3	9.31	19.6
0.50	6.71	6.12	7.47				

<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>
0.120	1	0	4.72	1	0	6.81	1	0
0.370	1	0	4.89	1	0	7.02	1	0
0.570	1	0	5.31	1	0	7.22	2	1
0.720	1	0	5.39	1	0	7.27	3	2
0.830	1	0	5.49	2	1	7.36	1	0

<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>
1.53	1	0	5.51	1	0	7.40	1	1
1.74	1	0	5.52	1	0	7.43	2	1
1.80	1	0	5.53	1	0	7.46	1	0
2.55	1	0	5.54	1	1	7.47	1	0
2.78	1	0	5.55	2	1	7.48	1	1
3.11	1	0	5.58	2	0	7.50	3	3
3.65	1	0	6.07	1	1	7.53	1	1
3.69	1	0	6.11	1	0	7.62	2	1
3.78	5	0	6.19	1	1	7.74	1	1
3.84	3	0	6.20	1	0	7.97	1	1
3.85	3	0	6.40	1	0	8.20	1	1
3.99	1	0	6.47	1	1	8.63	1	1
4.08	1	0	6.52	1	1	9.27	1	1
4.47	1	0	6.64	1	0	14.4	1	1

**Totals**

**75    24**



**Modelocked/CW Study (CW) MVL - 24hr**  
**A13 OS, A39 OS, C03 OS, C91 OD, C63 OD**

ONES = 29                  ZEROES = 45                  TOTAL = 74

Percent confidence = 0.95

ED50 = 5.84    Upper FL = 6.58                  Lower FL = 5.23

Intercept = -6.14                  Slope = 8.01

Pearson's Chi-Sq = 49.7143    Probability of Chi-Sq = 0.8001

h = 1.00                  g = 0.19                  t = 1.96

Log XBAR = 0.758                  Log YBAR = 4.93

SY Y = 70.134 SXY = 2.549    SXX = 0.318    S0 = 30.186

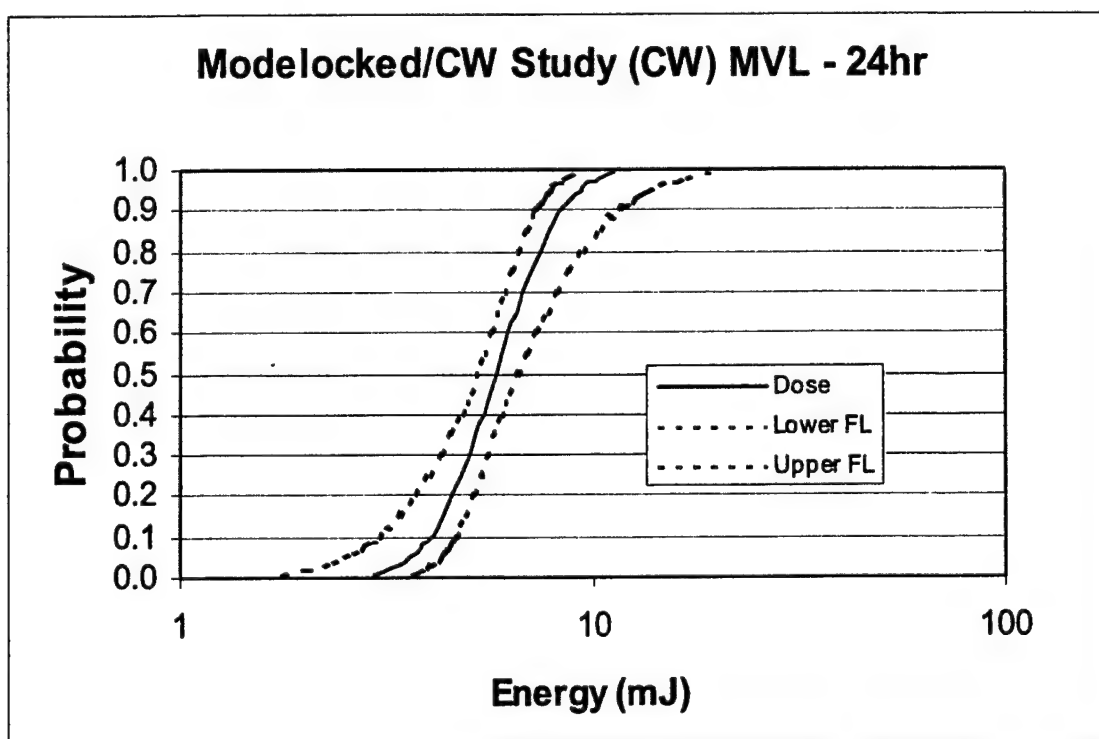
<u>Prob</u>	<u>Dose</u>	<u>LFL</u>	<u>UFL</u>	<u>Prob</u>	<u>Dose</u>	<u>LFL</u>	<u>UFL</u>
0.01	2.99	1.79	3.71	0.55	6.05	5.45	6.90
0.02	3.24	2.05	3.93	0.60	6.28	5.67	7.26
0.03	3.40	2.23	4.07	0.65	6.52	5.88	7.68
0.04	3.53	2.38	4.19	0.70	6.79	6.10	8.17
0.05	3.64	2.51	4.28	0.75	7.09	6.34	8.75
0.06	3.74	2.62	4.37	0.80	7.44	6.60	9.46
0.07	3.82	2.73	4.44	0.85	7.87	6.90	10.4
0.08	3.90	2.82	4.51	0.90	8.44	7.29	11.7
0.09	3.97	2.91	4.57	0.91	8.58	7.38	12.0
0.10	4.04	3.00	4.64	0.92	8.75	7.49	12.4
0.15	4.34	3.37	4.90	0.93	8.92	7.60	12.9
0.20	4.58	3.69	5.13	0.94	9.13	7.73	13.4
0.25	4.81	3.99	5.35	0.95	9.37	7.88	14.0
0.30	5.02	4.26	5.57	0.96	9.66	8.06	14.7
0.35	5.23	4.52	5.79	0.97	10.0	8.29	15.7
0.40	5.43	4.77	6.03	0.98	10.5	8.59	17.1
0.45	5.63	5.01	6.29	0.99	11.4	9.10	19.6
0.50	5.84	5.23	6.58				

<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>	<u>Dose</u>	<u>Tries</u>	<u>Hits</u>
0.150	1	0	4.25	1	0	7.05	1	1
0.380	1	0	4.54	1	0	7.09	1	1
0.400	1	0	4.56	1	0	7.10	2	2
0.700	1	0	4.60	1	0	7.25	1	1
0.740	1	0	4.76	1	0	7.45	1	1

Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
1.40	1	0	4.91	1	0	7.47	1	1
1.89	1	0	5.24	1	1	7.48	1	1
1.94	1	0	5.43	1	1	7.50	1	1
2.94	1	0	5.45	3	2	7.52	1	0
3.24	1	0	5.47	3	0	7.53	1	1
3.42	1	0	5.50	1	0	7.58	1	1
3.43	1	0	5.53	3	1	7.61	1	0
3.67	1	0	5.55	1	0	7.65	1	1
3.78	4	1	5.58	1	0	7.74	1	0
3.79	1	0	5.77	1	0	7.75	1	1
3.80	1	1	5.99	1	0	7.80	1	1
3.86	2	0	6.15	1	1	7.85	1	1
3.87	1	0	6.27	1	1	9.02	1	1
3.90	2	0	6.34	2	1	11.7	1	1
4.02	1	0	6.38	1	1			
4.06	1	0	6.69	1	1			

**Totals**

**74 29**



**Modelocked/CW Study (CW) FAVL - 24hr**  
**A13 OS, A39 OS, C03 OS, C91 OD, C63 OD**

ONES = 27                      ZEROES = 47                      TOTAL = 74

Percent confidence = 0.95

ED50 = 6.04    Upper FL = 6.89                      Lower FL = 5.41

Intercept = -6.00                      Slope = 7.68

Pearson's Chi-Sq = 51.0225    Probability of Chi-Sq = 0.7606

h = 1.00                      g = 0.20                      t = 1.96

Log XBAR = 0.764                      Log YBAR = 4.87

SYX = 70.112    SXY = 2.487    SXX = 0.324    S0 = 30.558

Prob	Dose	LFL	UFL	Prob	Dose	LFL	UFL
0.01	3.01	1.73	3.75	0.55	6.27	5.63	7.26
0.02	3.26	2.00	3.98	0.60	6.52	5.86	7.69
0.03	3.44	2.19	4.14	0.65	6.78	6.08	8.17
0.04	3.57	2.35	4.26	0.70	7.07	6.31	8.74
0.05	3.69	2.48	4.36	0.75	7.39	6.56	9.42
0.06	3.79	2.60	4.45	0.80	7.77	6.83	10.3
0.07	3.88	2.71	4.53	0.85	8.24	7.15	11.3
0.08	3.96	2.82	4.60	0.90	8.87	7.56	12.9
0.09	4.04	2.91	4.67	0.91	9.03	7.66	13.3
0.10	4.11	3.00	4.73	0.92	9.21	7.78	13.8
0.15	4.43	3.41	5.01	0.93	9.40	7.90	14.3
0.20	4.69	3.76	5.26	0.94	9.63	8.04	14.9
0.25	4.93	4.08	5.50	0.95	9.89	8.20	15.6
0.30	5.16	4.37	5.74	0.96	10.2	8.39	16.5
0.35	5.38	4.65	5.99	0.97	10.6	8.63	17.7
0.40	5.60	4.92	6.26	0.98	11.2	8.96	19.4
0.45	5.82	5.17	6.56	0.99	12.1	9.50	22.5
0.50	6.04	5.41	6.89				

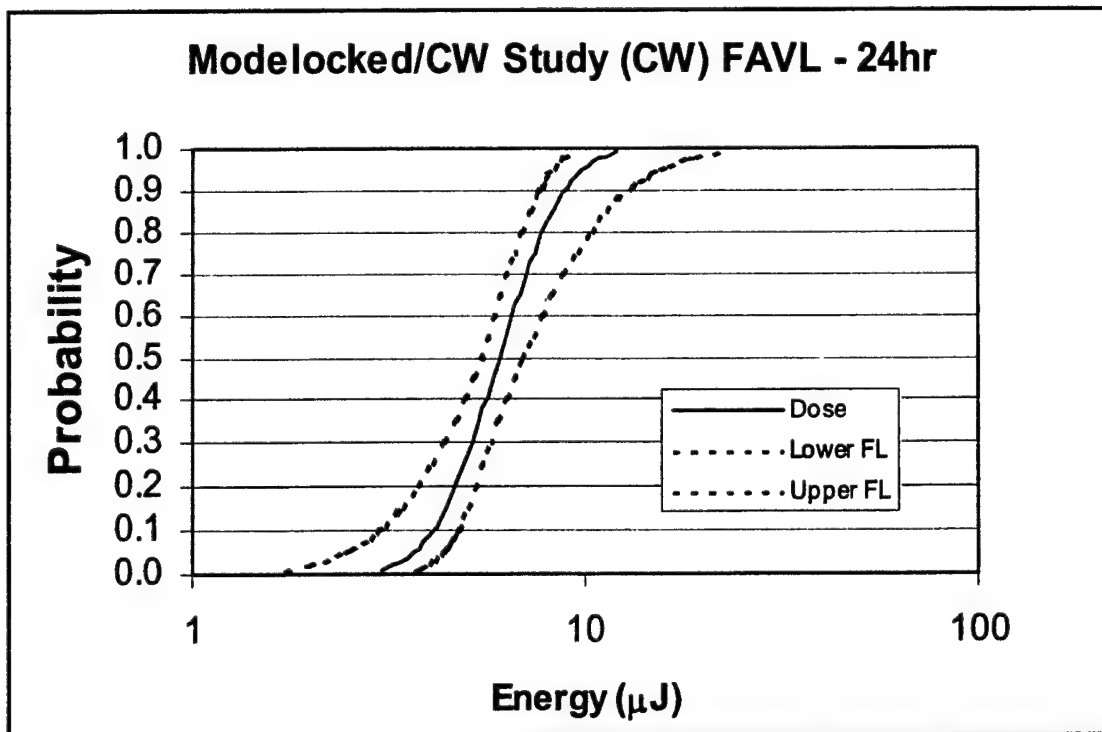
Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
0.150	1	0	4.25	1	0	7.05	1	1
0.380	1	0	4.54	1	0	7.09	1	1
0.400	1	0	4.56	1	0	7.10	2	2
0.700	1	0	4.60	1	0	7.25	1	1
0.740	1	0	4.76	1	0	7.45	1	1



Dose	Tries	Hits	Dose	Tries	Hits	Dose	Tries	Hits
1.40	1	0	4.91	1	0	7.47	1	1
1.89	1	0	5.24	1	0	7.48	1	0
1.94	1	0	5.43	1	0	7.50	1	1
2.94	1	0	5.45	3	1	7.52	1	0
3.24	1	0	5.47	3	1	7.53	1	1
3.42	1	0	5.50	1	0	7.58	1	1
3.43	1	0	5.53	3	1	7.61	1	0
3.67	1	1	5.55	1	0	7.65	1	1
3.78	4	1	5.58	1	0	7.74	1	0
3.79	1	0	5.77	1	0	7.75	1	1
3.80	1	0	5.99	1	1	7.80	1	1
3.86	2	0	6.15	1	1	7.85	1	1
3.87	1	0	6.27	1	1	9.02	1	1
3.90	2	0	6.34	2	1	11.7	1	1
4.02	1	0	6.38	1	1			
4.06	1	0	6.69	1	1			

**Totals**

**74 27**

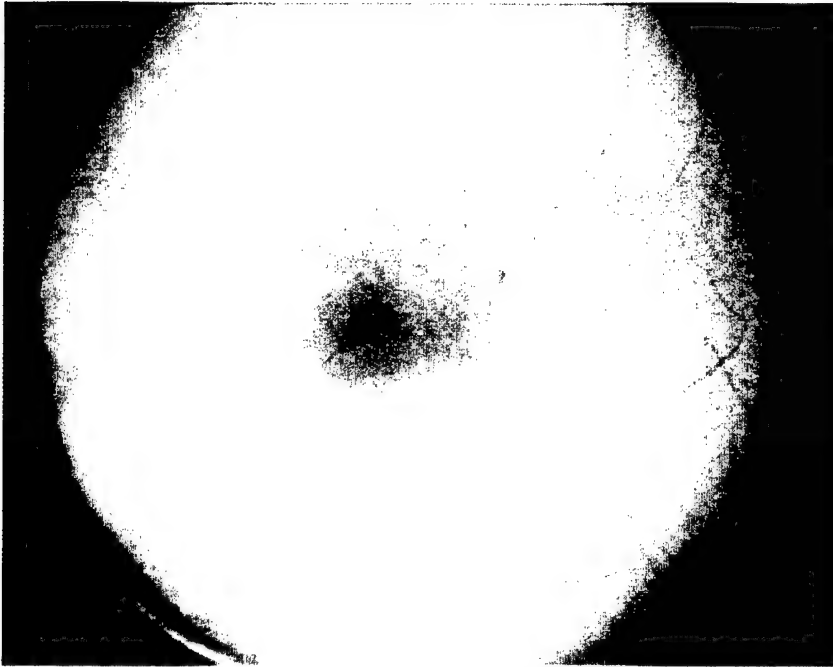


## APPENDIX II

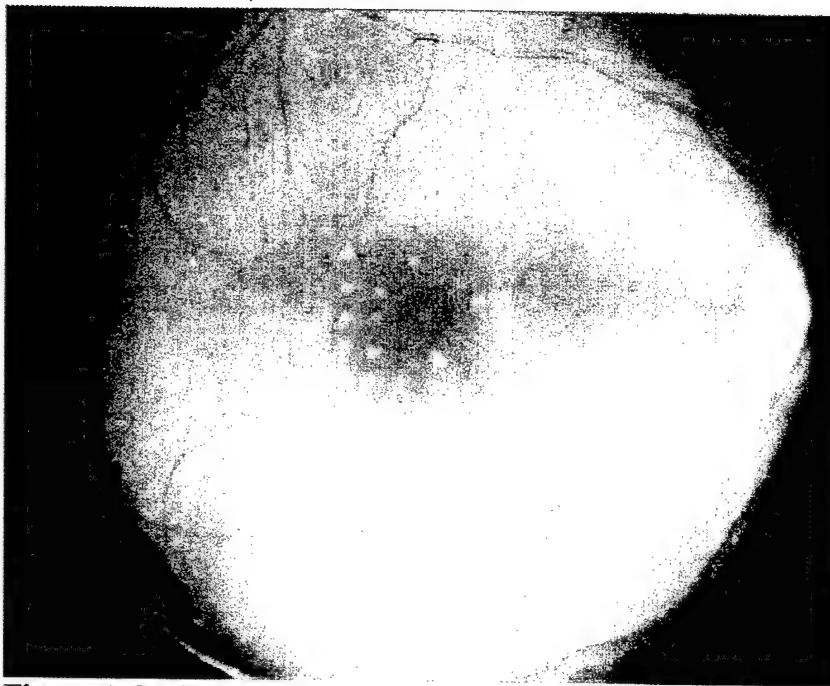
This appendix contains fundus photographs showing visible lesion development and fluorescein angiography for representative data from each study. Table A-1 contains a summary of the photographs included along with the laser exposure parameters and read times. We have attempted to include at least one figure from each type of laser exposure conducted in the study.

Figure	Date	Subject	Eye	Pulse Width	Wavelength	Read Time	Study
A -1	18-Oct-95	995z	OS	7ns	1064nm	24hr	IR
A -2	25-Oct-95	A13z	OD	80ps	1064nm	24hr	IR
A -3	13-Mar-96	A35z	OS	20ps	1064nm	24hr	IR
A -4	22-Apr-97	C03z	OS	1ps	1060nm	24hr	IR
A -5	14-Mar-97	C05z	OD	150fs	1060nm	24hr	IR
A -6	1-Apr-97	C11z	OD	150fs	1060nm	24hr	IR
A -7	31-Jul-97	C47z	OD	100fs	530nm	24hr	IR
A -8	6-May-97	C63z	OS	100fs	1060nm	24hr	Spotsizes
A -9	14-May-97	A39z	OS	150fs	1060nm	24hr	Spotsizes
A -10	27-Jun-97	C91z	OS	150fs	1060nm	24hr	Spotsizes
A -11	7-Jul-97	C91z	OD	150fs	1060nm	1hr	Spotsizes
A -12	17-Nov-97	C77z	OD	150fs	1060nm	24hr	Spotsizes
A -13	20-Nov-97	C77z	OS	150fs	1060nm	24hr	Spotsizes
A -14	25-Feb-97	B84z	OS	130fs	800nm	24hr	Mac-Para
A -15	19-Aug-98	D01z	OS-p	130fs	800nm	24hr	MultiPulse
A -16	28-Jul-98	C05z	OD-p	130fs	800nm	24hr	MultiPulse
A -17	19-May-98	A11z	OS-p	130fs	800nm	24hr	MultiPulse
A -18	2-Jun-98	A39z	OD-p	130fs	800nm	24hr	MultiPulse
A -19	8-Jul-98	C15z	OD-p	130fs	800nm	24hr	MultiPulse
A -20	12-Jan-99	C03z	OS-p	130fs	800nm	24hr	ML-CW
A -21	15-Dec-98	A39z	OS-p	109fs	800nm	24hr	ML-CW
A -22	8-Dec-98	A13z	OS-p	110fs	800nm	24hr	ML-CW

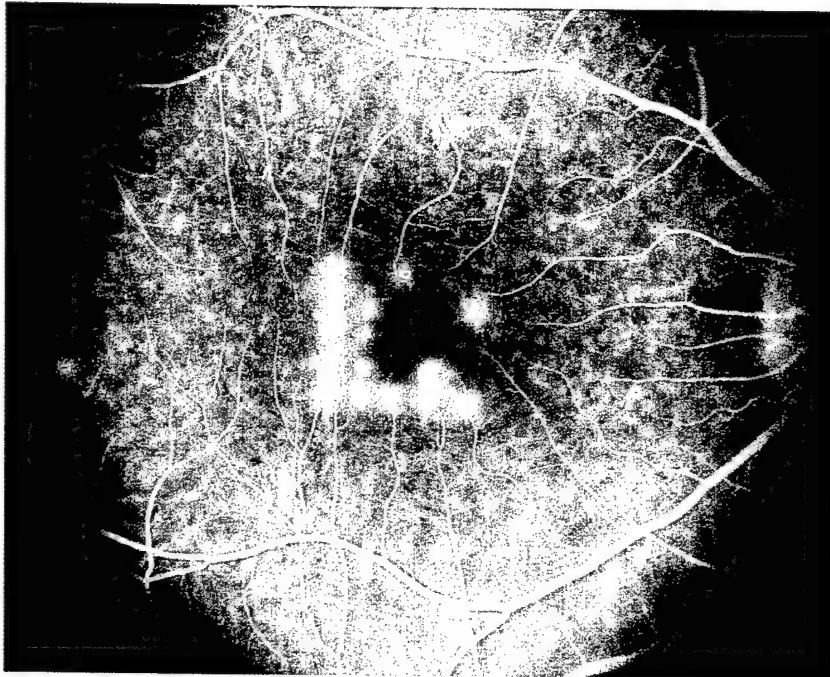
Table A-1. Summary of photos contained within Appendix II.



**Figure A-1.** 995z OS – 18 Oct 95 – 24-hour post-exposure.  
IR Study, 1064-nm, 7-ns pulses, energy range 14.8 - 188 $\mu$ J, 20 exposures, 2  
test shots below



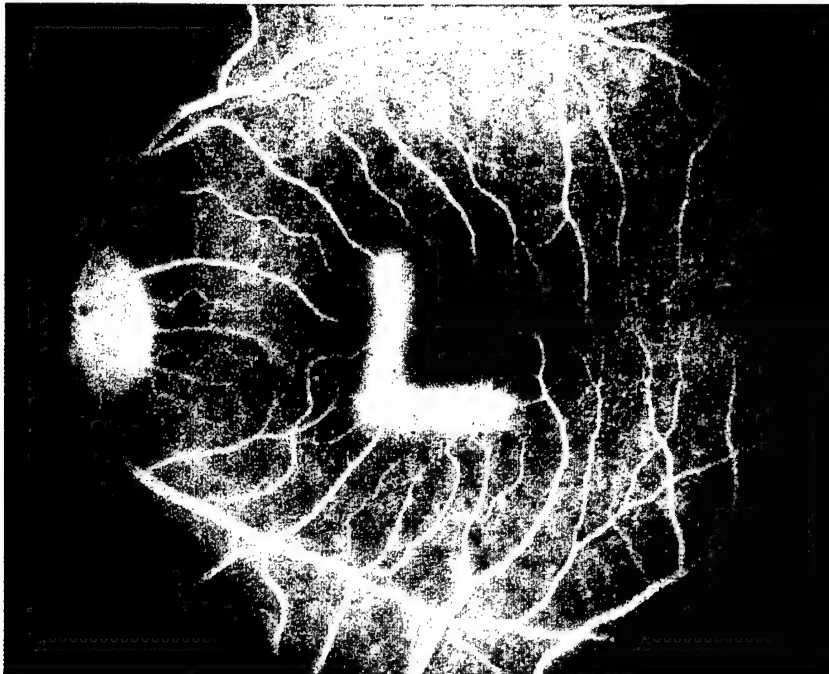
**Figure A-2.** A13z OD – 25 Oct 95 – 24-hour post-exposure  
IR Study, 1064-nm, 80-ps pulses, energy range 0.6 - 40.19 $\mu$ J, 16 exposures



**Figure A-2.** Fluorescence Angiography, A13z OD – 25 Oct 95 – 24-hour post-exposure



**Figure A-3.** A35z OS – 13 Mar 96 – 24-hour post-exposure  
IR Study, 1064-nm, 20-ps pulses, energy range 0.5 - 16.6 $\mu$ J, 25 exposures



**Figure A-3.** Fluorescence Angiography, A35z OS – 13 Mar 96 – 24-hour post-exposure

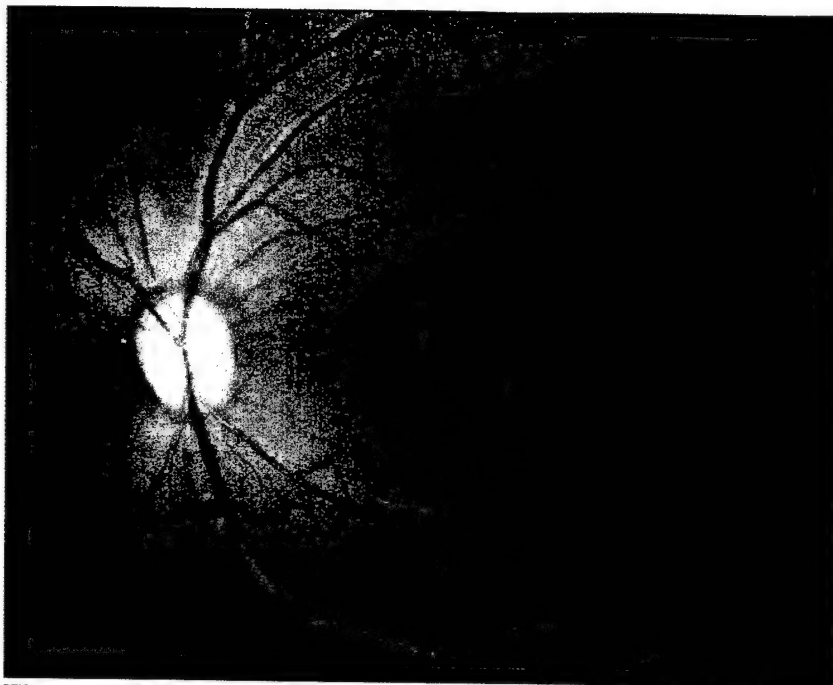


Figure A-4. C03z OS – 22 Apr 97 – 24-hour post-exposure  
IR Study, 1060-nm, 1-ps pulses, energy range 0.55 - 4.7 $\mu$ J, 25 exposures

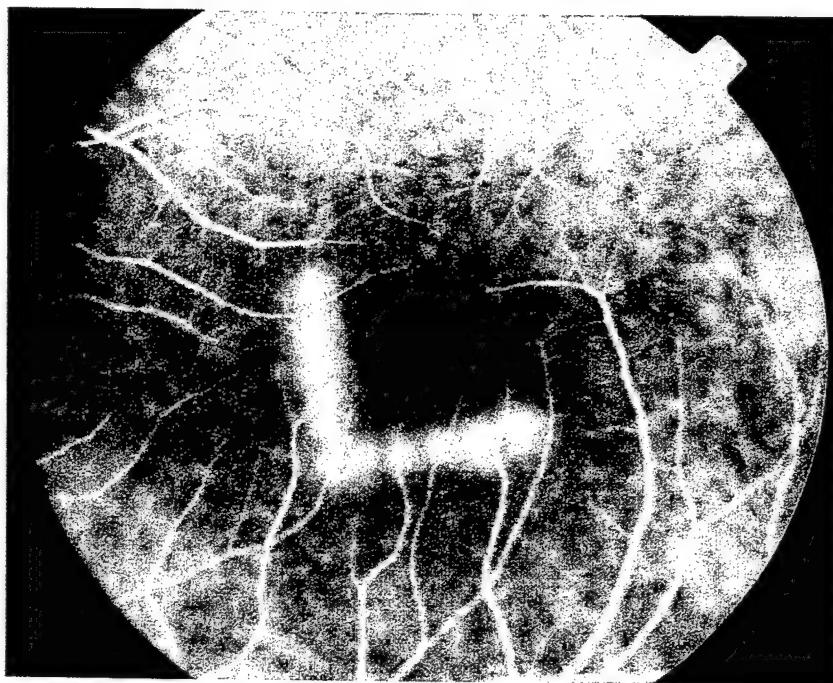
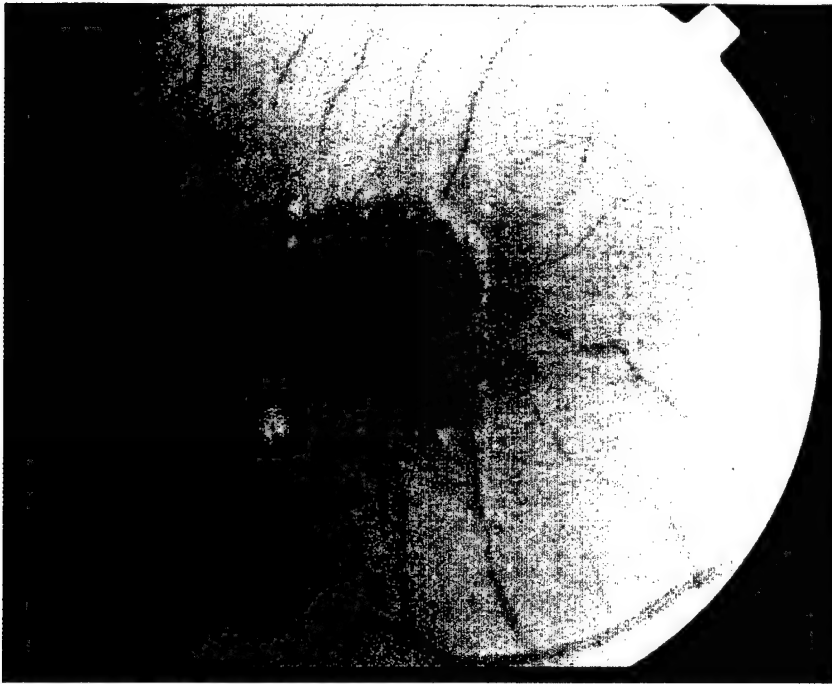
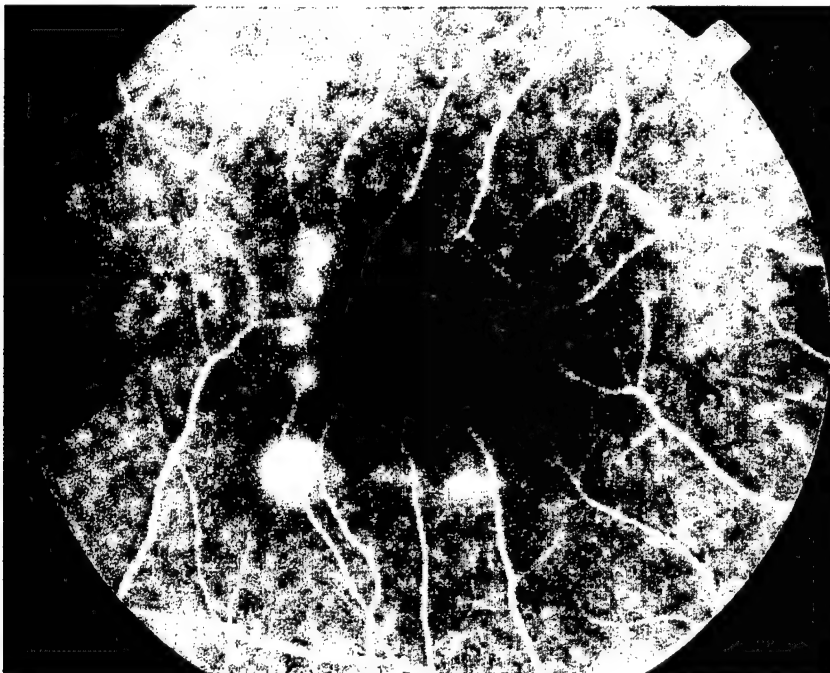


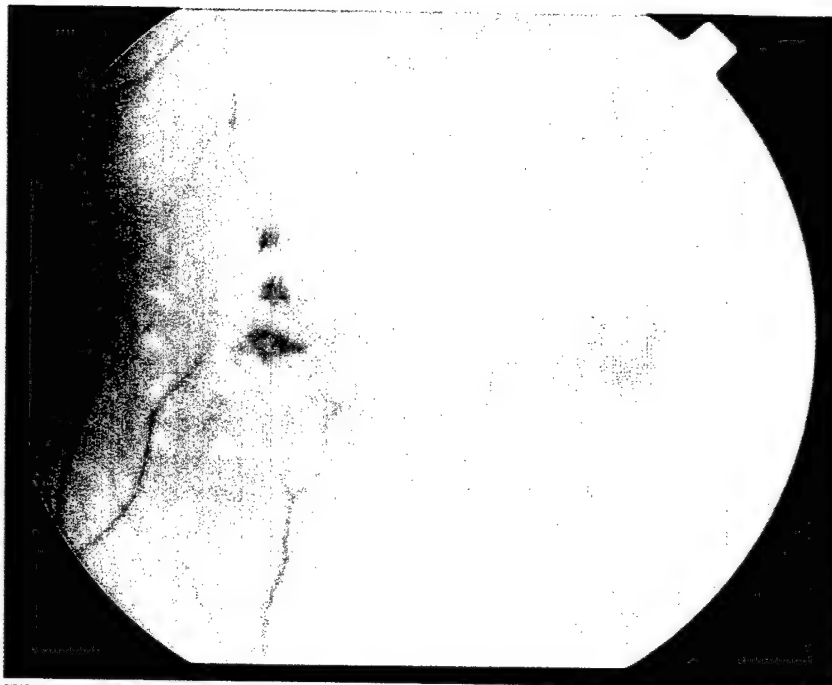
Figure A-4. Fluorescence Angiography, C03z 22 Apr97 OS 1ps 1060 24hr



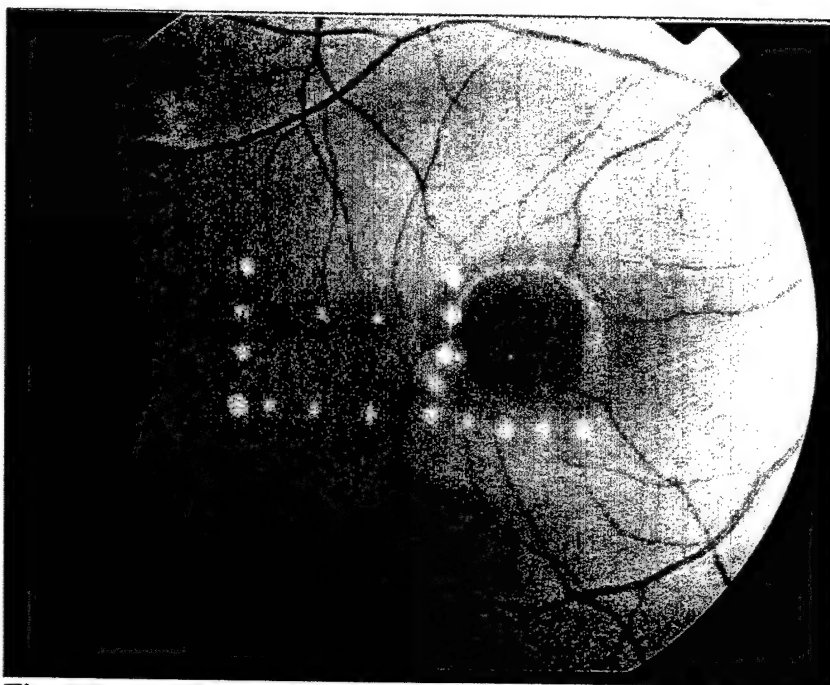
**Figure A-5.** C05z OD – 14 Mar 97 – 24-hour post-exposure  
IR Study, 1060-nm, 150-fs pulses, energy range 0.002 - 3.73 $\mu$ J, 25 exposures



**Figure A-5.** Fluorescence Angiography, C05z 14Mar97 OD 150fs 1060nm 24hr

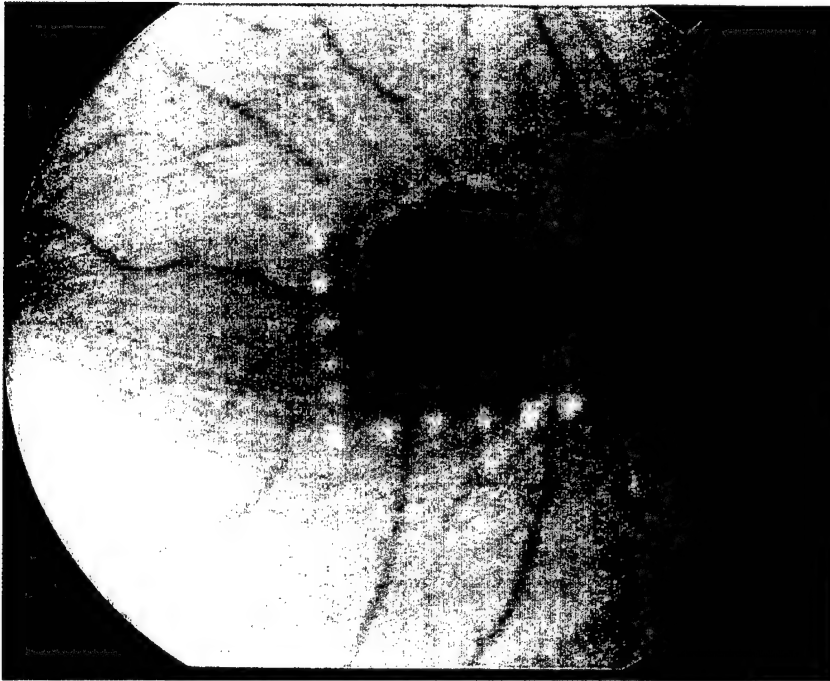


**Figure A-6.** C11z OD – 1 Apr 97 – 24-hour post-exposure  
IR Study, 1060-nm, 150-fs pulses, energy range 3.168 - 36.036 $\mu$ J, 16  
paramacular exposures (Note hemorrhages)

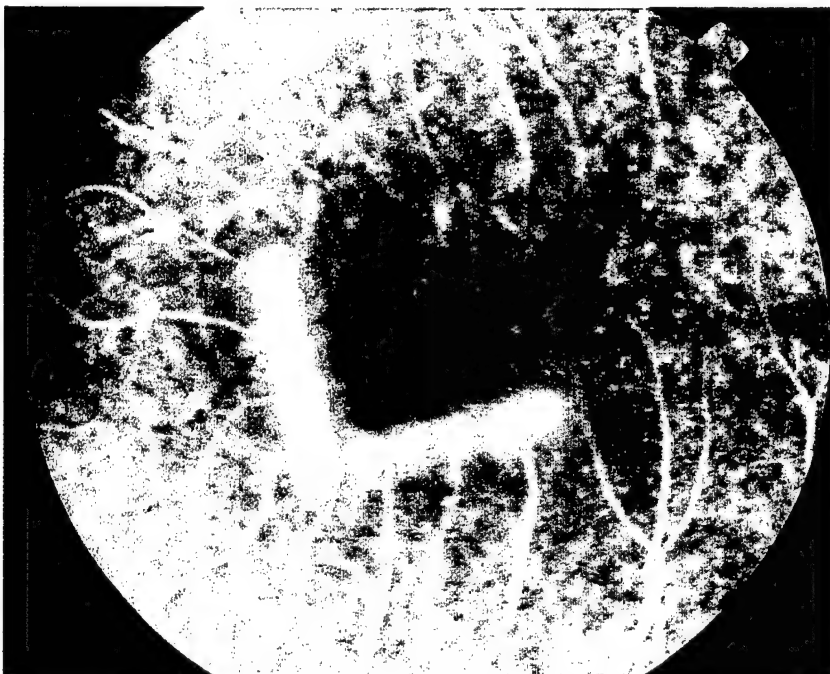


**Figure A-7.** C47z OD – 31 Jul 97 – 24-hour post-exposure  
IR Study, 530-nm, 100-fs pulses, energy range 0.193 - 22.41 $\mu$ J, 9  
paramacular exposures (Note hemorrhage)

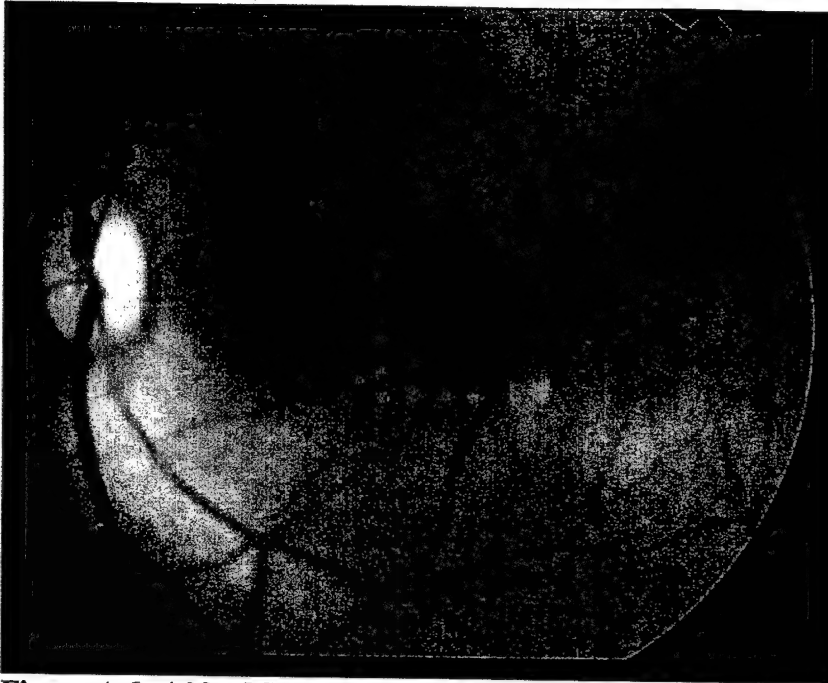




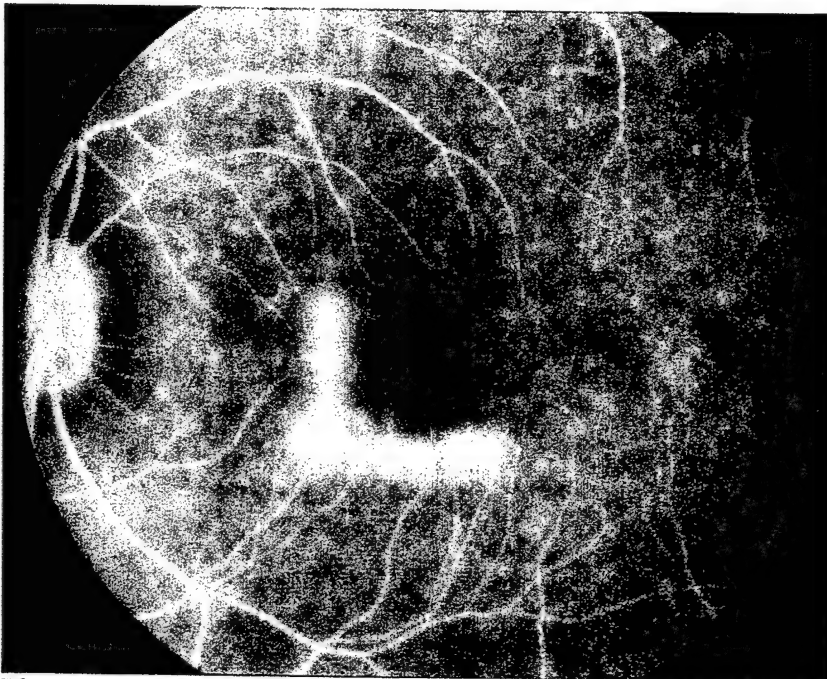
**Figure A-8.** C63z OS – 6 May 97 – 24-hour post-exposure  
 Spotsize Study, 1060-nm, 100-fs pulses, energy range 0.03 - 7.3 $\mu$ J, 25  
 macular exposures, 0.75 diopter



**Figure A-8.** Fluorescence Angiography, C63z 6May97 OS 100fs 1060nm 24hr Spotsize



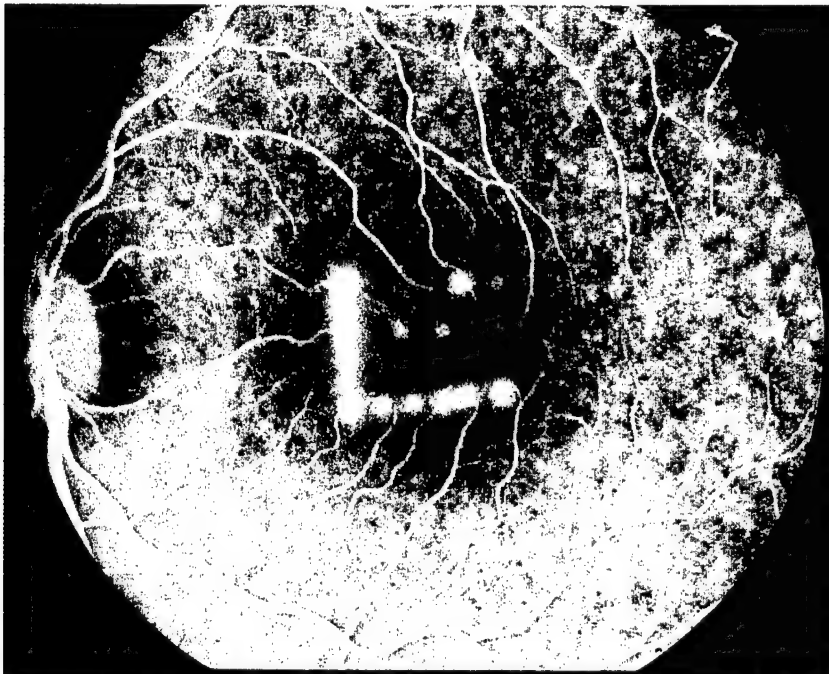
**Figure A-9.** A39z OS – 14 May 97 – 24-hour post-exposure  
Spotsize Study, 1060-nm, 150-fs pulses, energy range 0.01 – 24.6 $\mu$ J, 25  
macular exposures, -1.0 diopter



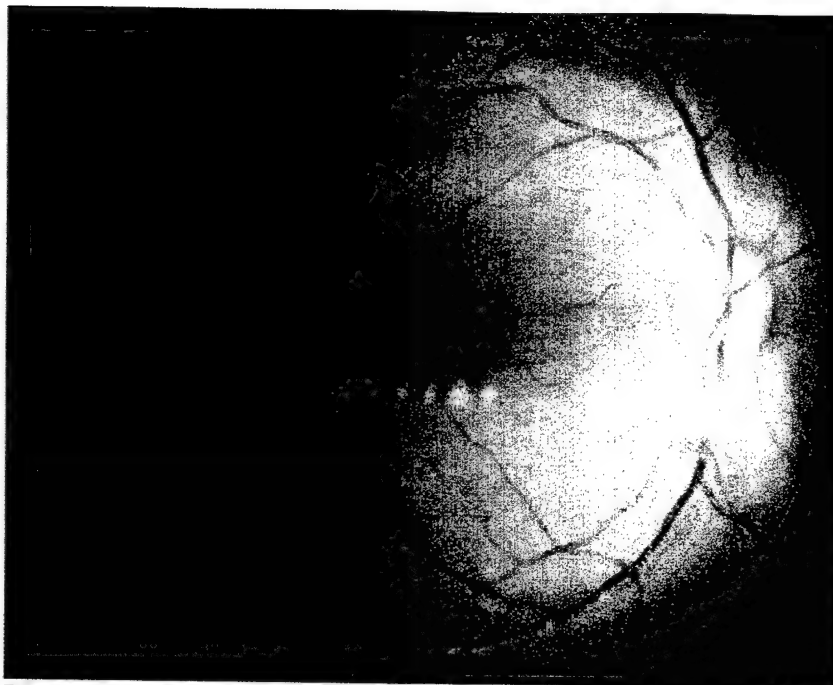
**Figure A-9.** Fluorescence Angiography, A39z 14May97 OS 150fs 1060nm 24hr Spotsize



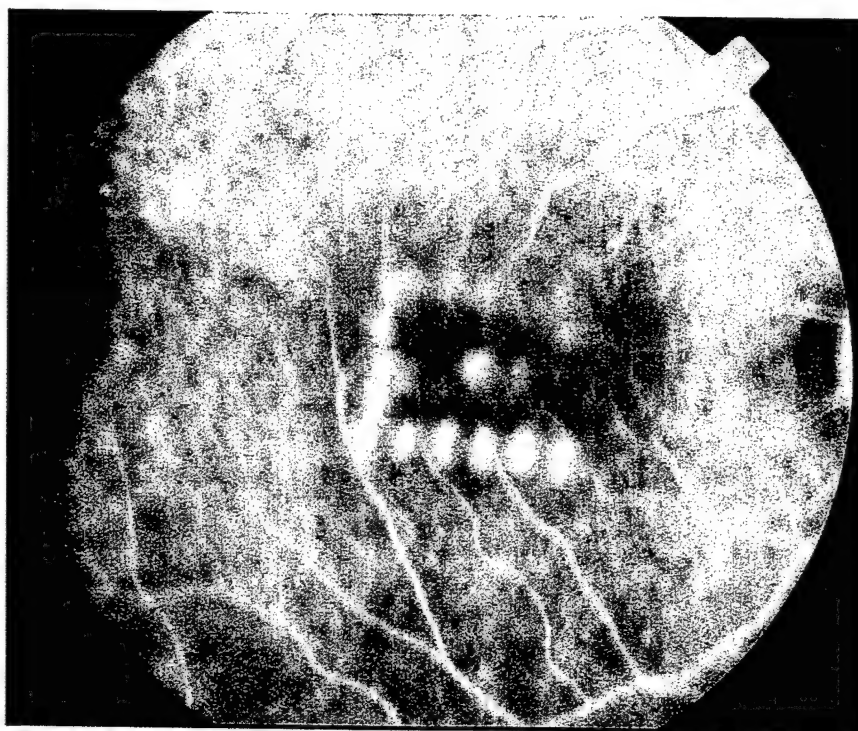
**Figure A-10.** C91z OS – 27 Jun 97 – 24-hour post-exposure  
 Spotsizes Study, 1060-nm, 150-fs pulses, energy range 0.01 – 36.1 $\mu$ J, 25 macular  
 exposures, -5.0 diopter



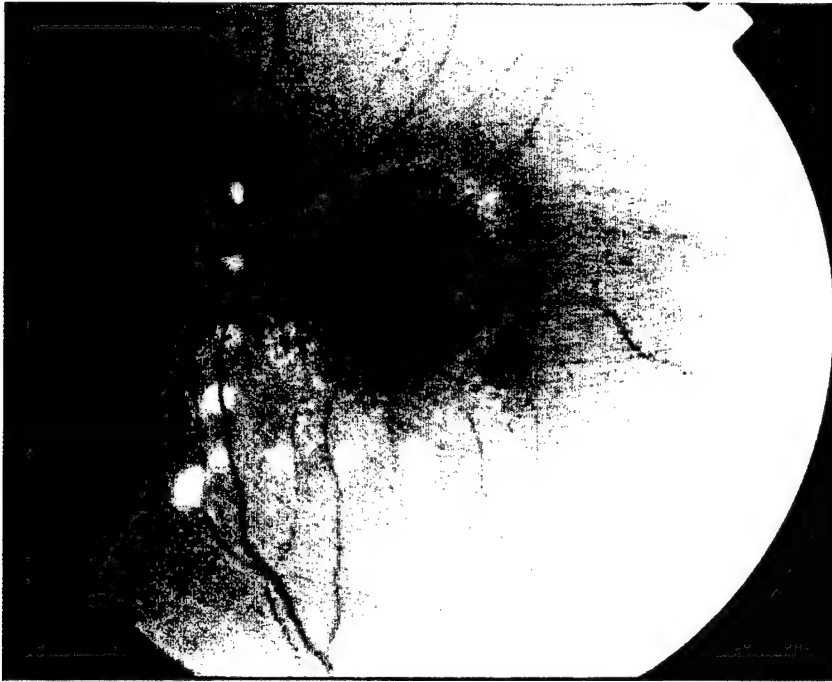
**Figure A-10.** Fluorescence Angiography, C91z OS 27Jun97 150fs 1060nm 24hr spotsizes



**Figure A-11.** C91z OD - 7 July 97 - 1-hour post-exposure  
 Spotsize Study, 1060-nm, 150-fs pulses, energy range 7.3 - 194 $\mu$ J, 20  
 macular exposures, -10.0 diopter



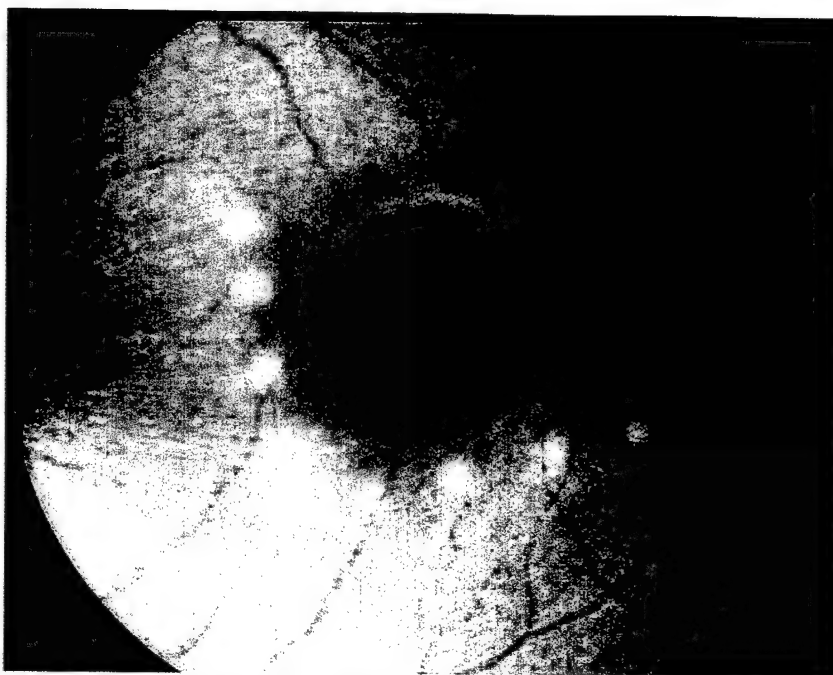
**Figure A-11.** Fluorescence Angiography, C91z OD - 7 July 97 - 1-hour  
 Spotsize Study, 1060-nm, 150-fs pulses



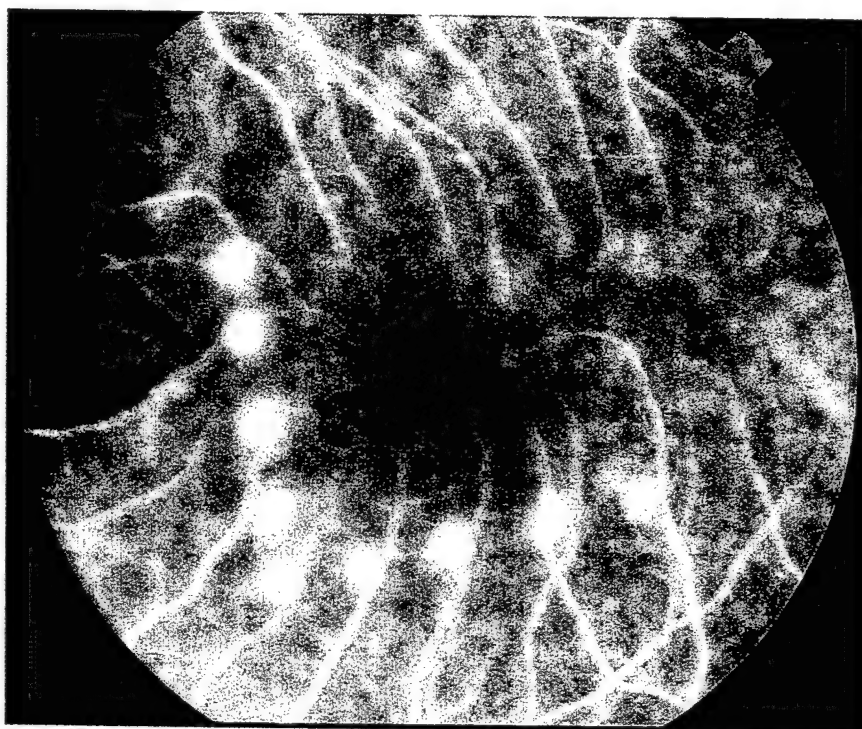
**Figure A-12.** C77z OD – 17 Nov 97 – 24-hour post-exposure  
 Spotsize Study, 1060-nm, 150-fs pulses, energy range 8.0 - 426 $\mu$ J, 16  
 macular exposures, Contact lens (note buckshot pattern)



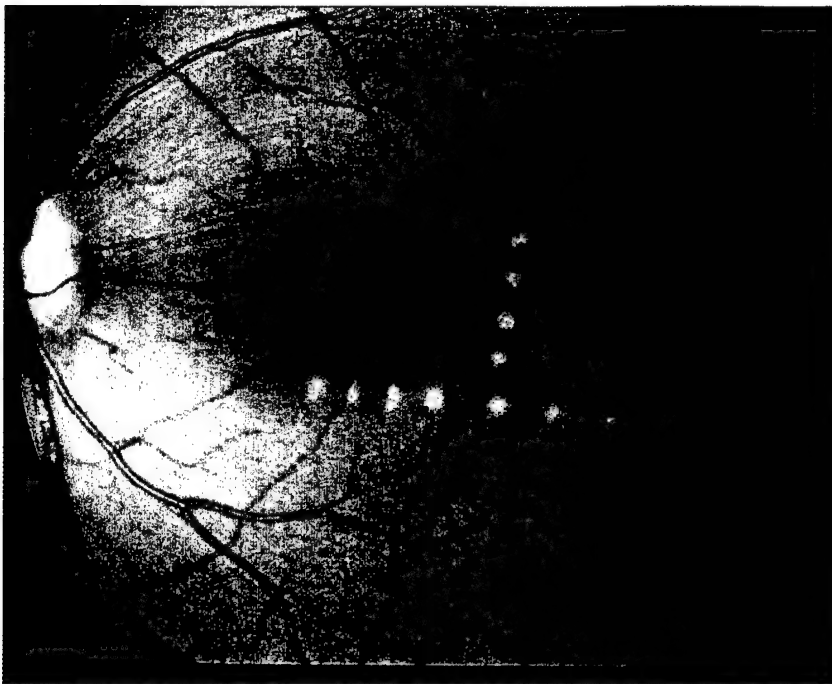
**Figure A-12.** Fluorescence Angiography, C77z OD – 17 Nov 97 – 24-hour post-exposure  
 Spotsize Study, 1060-nm, 150-fs pulses, energy range 8.0 - 426 $\mu$ J, 16  
 macular exposures, Contact lens (note buckshot pattern)



**Figure A-13.** C77z OS – 20 Nov 97 – 24-hour post-exposure  
 Spotszize Study, 1060-nm, 150-fs pulses, energy range 7.3 - 209 $\mu$ J, 16  
 macular exposures, contact lens (note buckshot pattern)

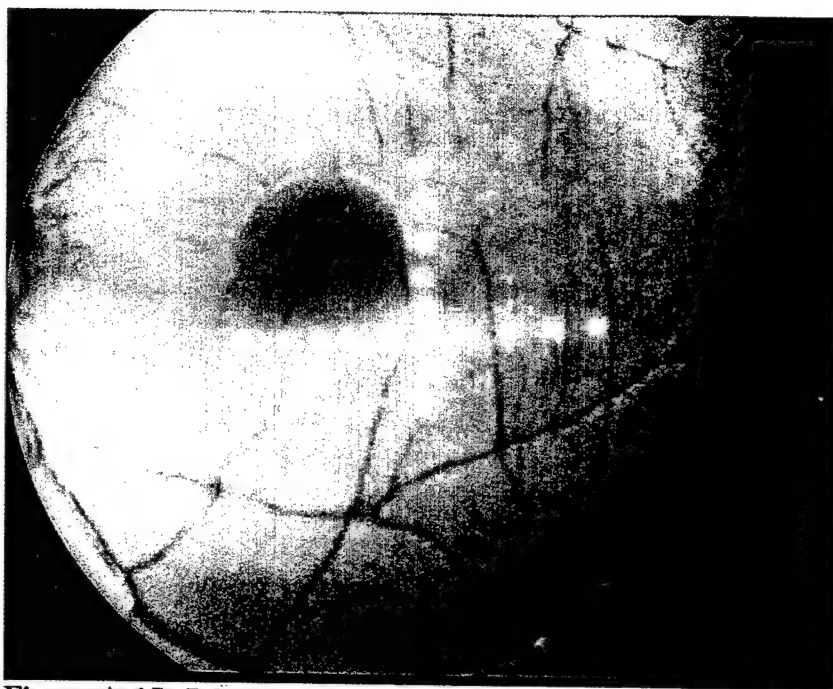


**Figure A-13.** Fluorescence Angiography, C77z OS – 20 Nov 97 – 24-hour post-exposure  
 Spotszize Study, 1060-nm, 150-fs pulses, energy range 7.3 - 209 $\mu$ J, 16  
 macular exposures, contact lens (note buckshot pattern)

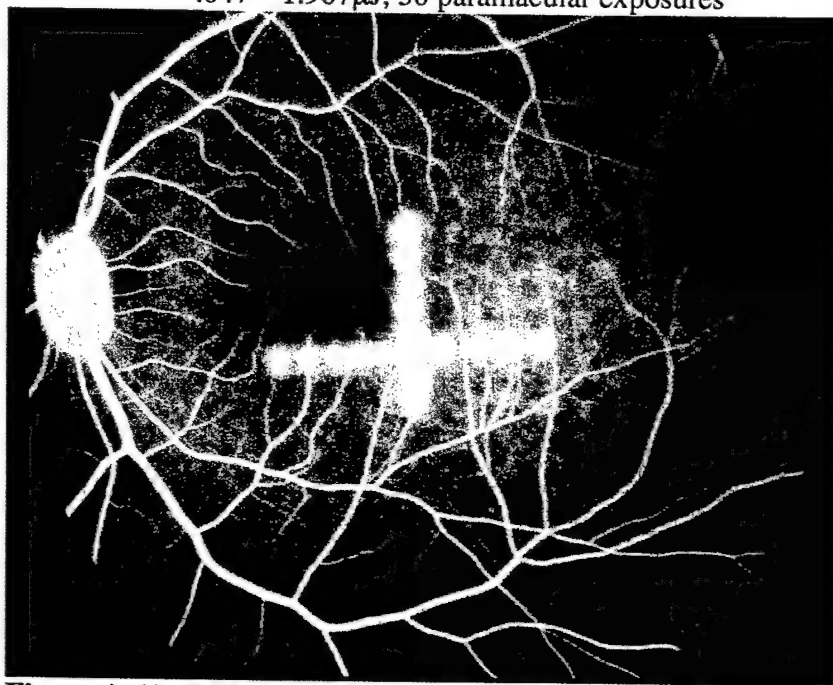


**Figure A-14.** B84z OS – 25 Feb 97 – 24-hour post-exposure  
Macular-Paramacular Study, 800-nm, 130-fs pulses, energy range 0.02 –  
3.98 $\mu$ J, 20 paramacular exposures





**Figure A-15.** D01z OS – 19 Aug 98 – 24-hour post-exposure  
Multiple-Pulse Study, 800-nm, 130-fs pulses, single pulse, energy range  
.047 – 1.967 $\mu$ J, 30 paramacular exposures

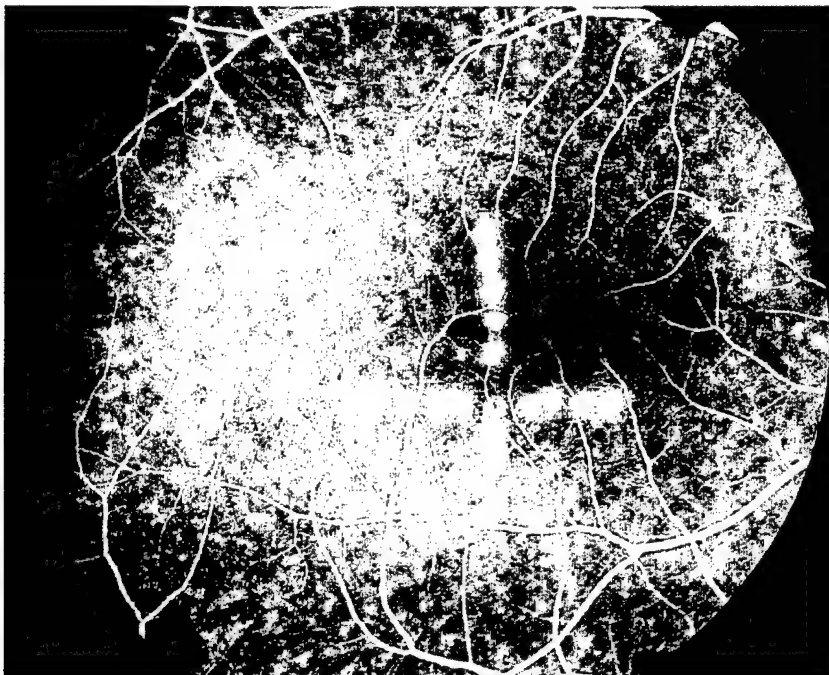


**Figure A-15.** Fluorescence Angiography, D01z OS – 19 Aug 98 – 24-hour post-exposure  
Multiple-Pulse Study, 800-nm, 130-fs pulses, single

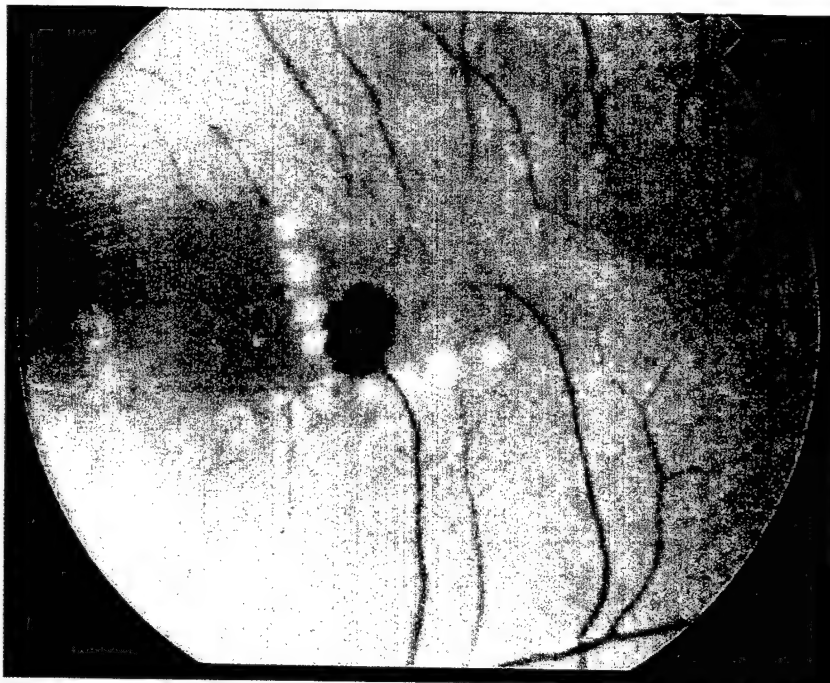




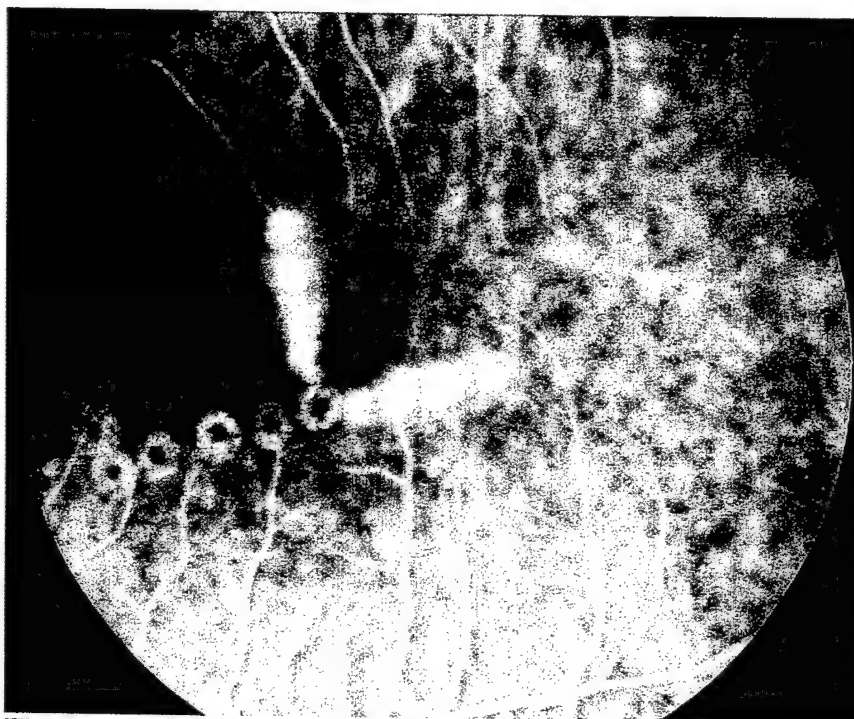
**Figure A-16.** C05z OD – 28 Jul 98 – 24-hour post-exposure  
Multiple-Pulse Study, 800-nm, 130-fs pulses, 10 pulses/spot, energy range  
0.035 – 2.44 $\mu$ J, 30 paramacular exposures



**Figure A-16.** Fluorescene Angiography, C05z OD – 28 Jul 98 – 24-hour post-exposure  
Multiple-Pulse Study, 800-nm, 130-fs pulses, 10 pulses/spot, energy range  
0.035 – 2.44 $\mu$ J, 30 paramacular exposures



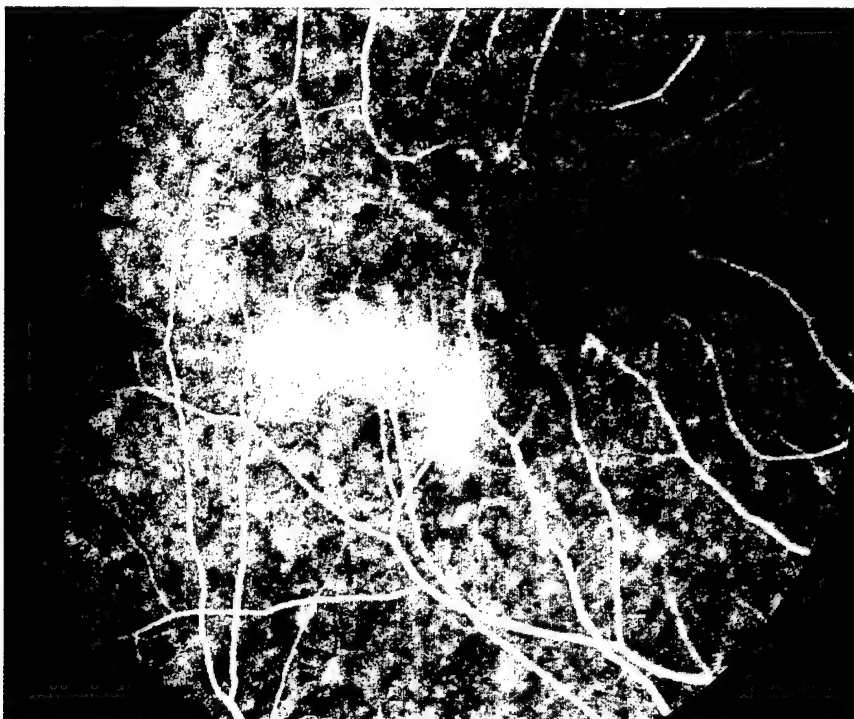
**Figure A-17.** A11z OS – 19 May 98 – 24-hour post-exposure  
Multiple-Pulse Study, 800-nm, 130-fs pulses, 100 pulses/spot, energy  
range .02 – .6 $\mu$ J, 16 paramacular exposures (Note hemorrhage)



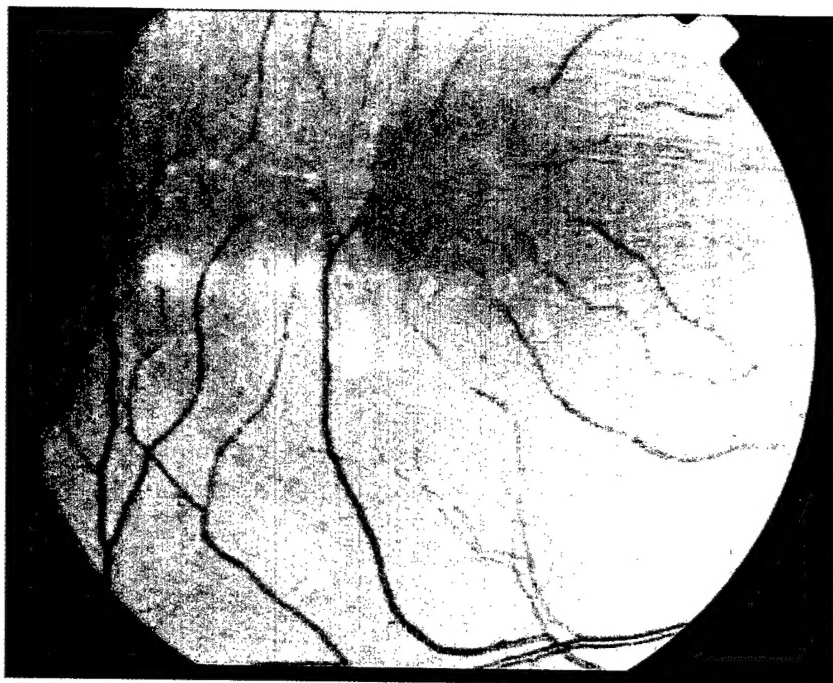
**Figure A-17.** Fluorescence Angiography, A11z OS – 19 May 98 – 24-hour post-exposure  
Multiple-Pulse Study, 800-nm, 130-fs pulses, 100 pulses/spot, energy  
range .02 – .6 $\mu$ J, 16 paramacular exposures (Note hemorrhage)



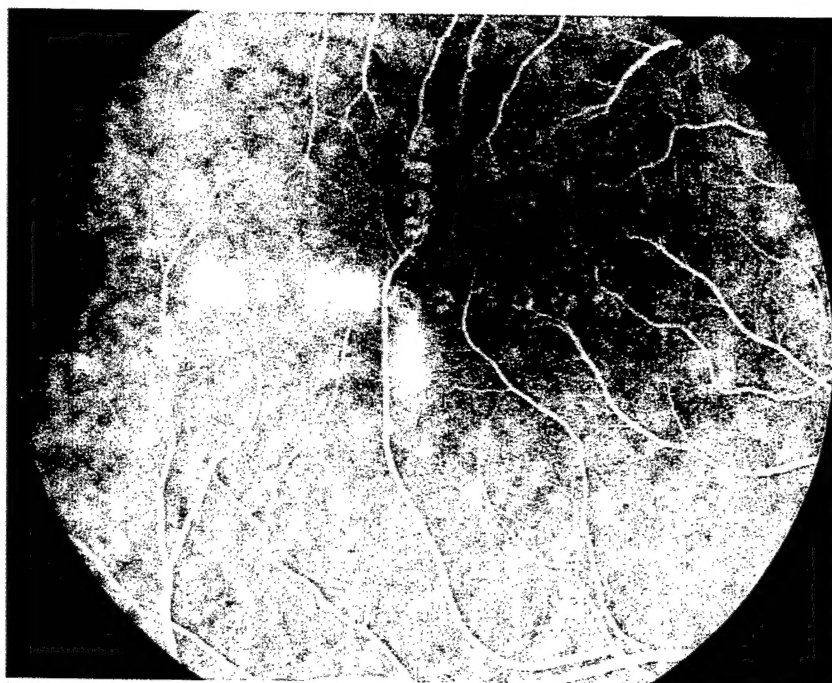
**Figure A-18.** A39z OD – 2 Jun 98 – 24-hour post-exposure  
Multiple-Pulse Study, 800-nm, 130-fs pulses, 1000 pulses/spot, energy  
range 0.0053 – 0.52 $\mu$ J, 26 paramacular exposures (Note hemorrhage)



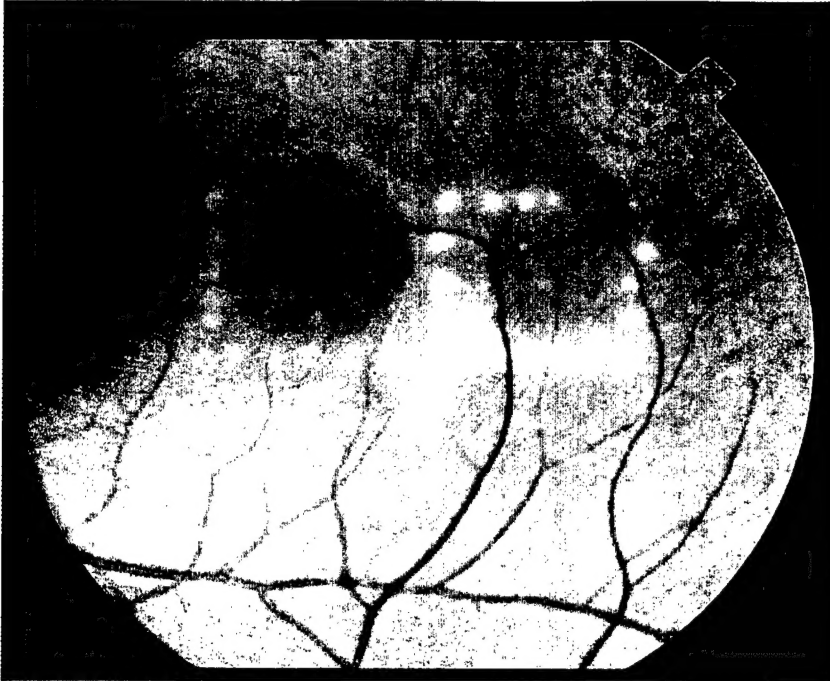
**Figure A-18.** A39z OD – 2 Jun 98 – 24-hour post-exposure  
Multiple-Pulse Study, 800-nm, 130-fs pulses, 1000 pulses/spot, energy  
range 0.0053 – 0.52 $\mu$ J, 26 paramacular exposures (Note hemorrhage)



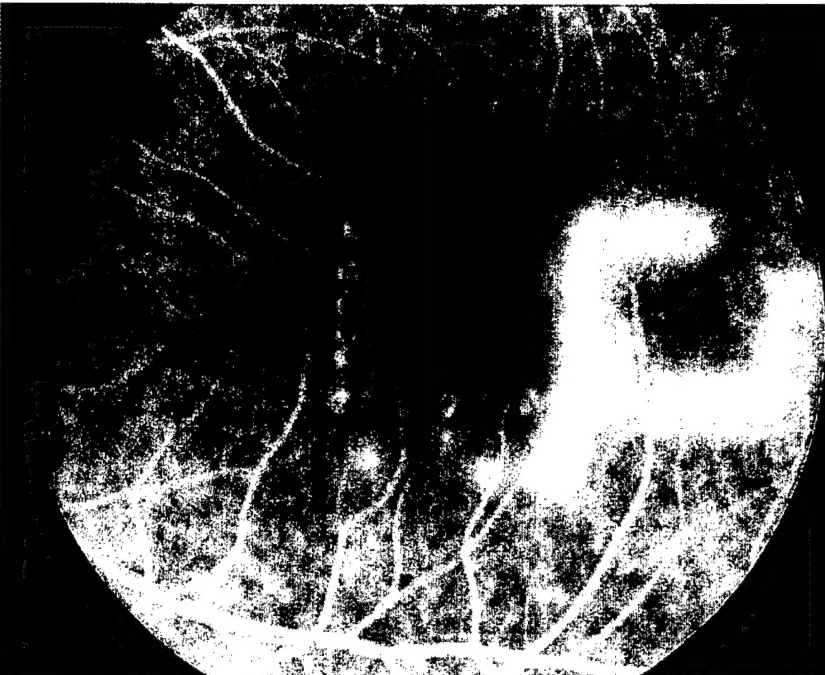
**Figure A-19.** C15z OD – 8 Jul 98 – 24-hour post-exposure  
Multiple-Pulse Study, 800-nm, 130-fs pulses, 10000 pulses/spot, energy  
range 0.009 - .682 $\mu$ J, 35 paramacular exposures



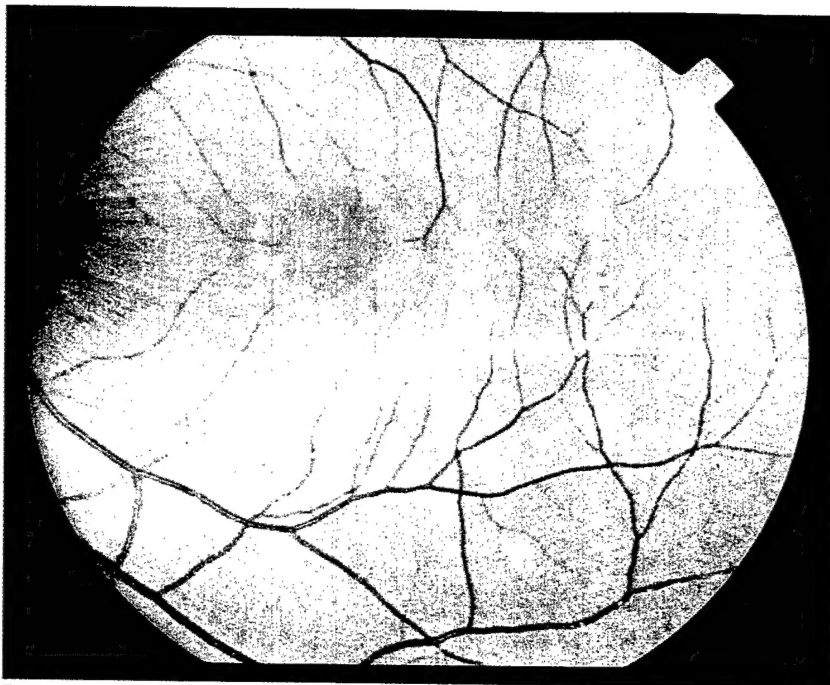
**Figure A-19.** Fluorescene Angiography, C15z OD – 8 Jul 98 – 24-hour post-exposure  
Multiple-Pulse Study, 800-nm, 130-fs pulses, 10000 pulses/spot, energy  
range 0.009 - .682 $\mu$ J, 35 paramacular exposures



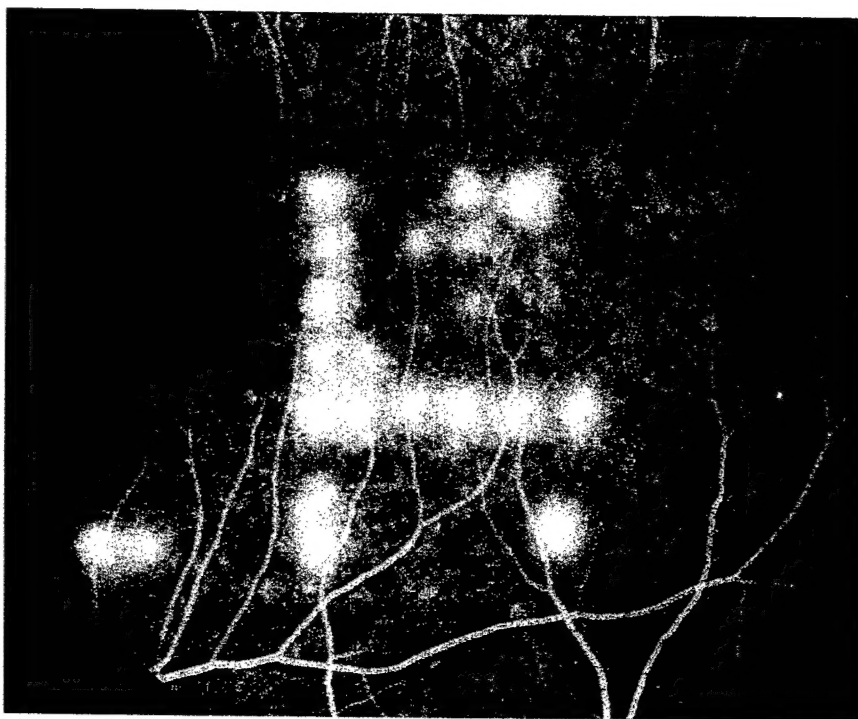
**Figure A-20.** C03z OS – 12 Jan 99 – 24-hour post-exposure  
Modelock/CW Study, 800-nm, 130-fs pulses, energy range 4.6 – 9.27mJ,  
30 paramacular exposures



**Figure A-20.** Fluorescene Angiography, C03z OS – 12 Jan 99 – 24-hour post-exposure  
Modelock/CW Study, 800-nm, 130-fs pulses, energy range 4.6 – 9.27mJ,  
30 paramacular exposures



**Figure A-21.** A39z OS – 15 Dec 98 – 24-hour post-exposure  
Modelock/CW Study, 800-nm, 109-fs pulses, energy range 1.74 – 7.85mJ,  
30 paramacular exposures



**Figure A-21.** Fluorescence Angiography, A39z OS – 15 Dec 98 – 24-hour post-exposure  
Modelock/CW Study, 800-nm, 109-fs pulses, energy range 1.74 – 7.85mJ,  
30 paramacular exposures





**Figure A-22.** A13z OS – 8 Dec 98 – 24-hour post-exposure  
Modelock/CW Study, 800-nm, 110-fs pulses, energy range 0.12 – 14.4mJ,  
30 paramacular exposures